Keynote Address Program
100 Fulfilling the Promise of Molecular Medicine In Autism

Speaker: M. Bear*MIT*

100.00 Introduction/Autism Speaks Strategic Plan - Geraldine Dawson.

100.01 Fulfilling the Promise of Molecular Medicine In Autism. M. Bear*, *MIT*

Metabotropic glutamate receptors (mGluRs) have been implicated in a diverse variety of neuronal functions. Data indicate that exaggerated signaling through mGluR5 can account for multiple cognitive and syndromic features of fragile X syndrome, the most common inherited form of mental retardation and autism. Since a reduction of mGluR5 signaling can reverse fragile X phenotypes, these studies provide a compelling rationale for the use of mGluR5 antagonists for the treatment of fragile X and autism.

Invited Educational Symposium Program
101 Before, During and After Diagnosis and Phenotyping

Moderator: G. Dawson*Autism Speaks, UNC Chapel Hill*

Organizer: C. Lord*University of Michigan*

Speakers: T. Charman[1]S. L. Bishop[2]A. S. Carter[3]D. Fein[4](1)*Institute of Education, University of London*, (2)*Waisman Center, University of Wisconsin-Madison*, (3)*University of Massachusetts Boston*, (4)*University of Connecticut*

101.00 Social Emotional and Problem Behaviors in Children with Autism Spectrum Disorders: Associations with Child and Family Impairment. A. S. Carter*, C. K. Kraper, S. D. Rosenblum and F. Martinez-Pedraza, *University of Massachusetts Boston*

With greater attention to early detection and diagnosis of autism spectrum disorders (ASDS), an increasing number of young children are receiving early intervention services for the social and communicative impairments associated with these conditions. This is extremely important, as early intervention greatly improves long-term adaptation. Studies of older children suggest that many children and adolescents with ASD have co-occurring psychiatric disorders such as anxiety disorders. Moreover, impairment in ASDs may be exacerbated when other psychiatric conditions are present. Although some investigators have begun to report on temperamental variation and sensory problems in young children with ASD, there has been little attention to the extent to which co-occurring social-emotional and behavioral problems may associated with core ASD symptoms or with child and family impairment. The focus of this presentation is on internalizing, externalizing and dysregulation problems in very young children with ASD and their relation to child and family impairment. In addition, stability of behavior problems will be examined.

Data will be presented from a longitudinal study of approximately 100 toddlers with ASD and their parents. Toddlers were enrolled when they were between 18- to 33-months of age and seen at two annual follow-up visits. All children met criteria for ASD based on the Autism Diagnostic Interview, the Autism Diagnostic Observation Schedule (ADOS) and the clinical impression of an experienced clinician. Parents completed the Infant-Toddler Social and Emotional Assessment (ITSEA; Carter & Briggs-Gowan, 2006), and the Family Life Impairment scale. The ITSEA is a 166-item parent report questionnaire that measures social-emotional/behavioral problems and competencies in 1- to 3-year olds. The ITSEA assesses four broad domains of behavior (Internalizing, Externalizing, Dysregulation, and Competencies). Items are rated on a 3-point scale from 0=Not true/Rarely to 2=Very True/Often. The Family Life Impairment Scale (FLIS; Briggs-Gowan et al, 1997) is a parent-report scale that assesses the extent to which the parent perceives that their child's behavior, personality, or special needs limit the child's participation in typical family activities or negatively affect the parent.

Specific questions that will be addressed in this presentation include: (1) Are social-emotional and problem behaviors reported by mothers and fathers in the toddler and preschool period stable among children with ASDs? (2) Are social-emotional and problem behaviors correlated with core autism symptoms in this young age group? and (3) Controlling for core autism symptoms and cognitive functioning, do social-emotional and

behavior problems contribute uniquely to family impairment?

101.01 Comorbid Behavioural Psychopathology and Autism Severity: Same or Different?. T. Charman*[1], E. Simonoff[2], A. Pickles[3], C. R. G. Jones[1] and G. Baird[4], (1)*Institute of Education, University of London*, (2)*Institute of Psychiatry*, (3)*University of Manchester*, (4)*Guy's Hospital*

Autism spectrum disorders (ASDs) are now recognized to occur in ~1% of children and to be a major public health concern because of their early onset, lifelong persistence and the high levels of associated disability. However, little is known about the associated psychopathology that may contribute to the level of disability. Delineating psychiatric comorbidity in ASDs is important because it may identify targets for specific intervention that could reduce overall impairment and improve quality of life and also signpost similar or different biological or environmental aetiological factors to those that are well recognised for psychiatric conditions. For example, several recent studies have indicated that common genetic factors might influence both ASD and ADHD symptoms.

Our recent epidemiological report (Simonoff et al., 2008; *JAACAP*) using a standardised, structured parental interview the Child and Adolescent Psychiatry Assessment (CAPA) found that two-thirds of 10- to 14-year old children with an ASD had at least one other psychiatric disorder that was causing additional functional impairment over and above that due to ASD, roughly six times the rate in the general population. Forty percent of the sample met criteria for two disorders; the most common being social anxiety disorder, ADHD and oppositional defiant disorder. Unlike for child psychiatric disorders in the absence of ASD there were few associations between putative risk factors and associated psychopathology. We concluded that comorbid psychiatric disorder in ASDs is common and frequently multiple and should be routinely evaluated in the clinical assessment of this group.

101.02 Self-Report in Adolescents and Adults with ASD: Implications for Diagnostic Assessment and for Evaluation of the Broader Autism Phenotype. S. L. Bishop*[1], K. Gotham[2], M. M. Seltzer[1] and C. Lord[2], (1)*Waisman Center, University of Wisconsin-Madison*, (2)*University of Michigan*

As a result of rises in the prevalence and public awareness of ASD, more children than ever are entering adulthood with a diagnosis of ASD, and increasing numbers of adults are presenting for initial evaluations with concerns about ASD. However, because ASD is normally diagnosed during childhood, relatively little is known about assessment of adolescents and adults with the disorder. Most empirically derived assessment tools have been primarily validated for use in children with ASD. Parent report measures, which are central to assessment of ASD in children, may not always be appropriate for assessing older individuals. Thus, both in terms of measuring ASD symptoms, as well as evaluating comorbid psychopathology, more work is needed to establish best practice guidelines for assessment of adults with ASD.

Until recently, standardized self-report measures were not available for adolescents and adults with ASD. Unlike assessment of other types of adult psychopathology, such as mood and anxiety disorders, where standardized self-report measures are a primary component of diagnostic evaluations, self-report has not traditionally been part of assessment of ASD. There remains much work to be done in order to understand how best to employ self-report instruments in the assessment of individuals with ASD. It will be important to investigate the extent to which adolescents and adults with ASD can provide valid reports of their own symptoms, and whether certain types of self-report measures are better at ascertaining an individual's true level of impairment.

This presentation will explore the potential uses of self-report measures in adolescents and adults with ASD, including assessing ASD symptoms, evaluating comorbid psychiatric disorders, and obtaining information about quality of life. Recent findings from longitudinal investigations and from clinical samples will illustrate advantages and limitations of the use of self-report measures in adolescents and adults with ASD. Implications of these findings for conceptualizing and evaluating the broader autism phenotype will also be discussed.

101.03 Cognitive and Behavioral Profiles of Children Who Recover From Autism. D. Fein*, M. Barton, I. M. Eigsti, L. Naigles, M. Rosenthal, K. Tyson, E. Troyb and M. Helt, *University of Connecticut*

Although Autism Spectrum Disorders (ASD) are generally lifelong, scattered evidence over the past 30 years indicates that between 3% and 25%

of children can lose their ASD diagnosis and enter the normal range of cognitive, adaptive and social skills. Predictors of recovery include normal intelligence, receptive language, imitation, and motor development. Earlier age of diagnosis and treatment, and PDD-NOS rather than Autistic Disorder are also favorable. Seizures, mental retardation and genetic syndromes are unfavorable signs.

The purpose of our ongoing study is to document this phenomenon in a more rigorous way, explore any residual vulnerabilities, examine history and treatment factors, and assess structural and functional brain parameters in the "optimal outcome" children to see if they still show ASD features.

We will report on some cognitive testing and psychiatric co-morbidities in three groups: The "optimal outcome" (OO) group, a group with high-functioning autism (HFA), and a control group with typical development (TD), all matched for age and performance IQ. Age range of participants is 9-18.

On the Wechsler Abbreviated Intelligence Scales, the groups were matched for PIQ; there were then no significant differences on VIQ or any subtest. Furthermore, the intellectual functioning in all 3 groups was above average (mean IQ about 115). On the BRIEF (a parent report measure of executive functioning), the OO group was solidly average on every subscale. The TD group was also unimpaired on every scale, and tended to do somewhat better than average, consistent with their high IQ's. The HFA group, in contrast, showed elevated scores on shifting, emotional control, initiating, working memory, and self-monitoring.

Of 23 typical controls, 3 had a disorder diagnosable by the K-SADS (2 with phobias, and one with depression, all in the past). In contrast, both the HFA and OO groups showed significant psychopathologies: 11 of the 15 HFA subjects (73%) showed a diagnosable disorder, of which 9 were current. Prominent were depression, various forms of anxiety disorder, tics, ADHD, and ODD. In the OO group, 16 of the 22 subjects (73%) showed a diagnosable disorder, of which 8 were still current. Prominent were ADHD, ODD, tics, and phobias, with one case each of depression and ODD. Psychiatric co-morbidity was, therefore, strikingly similar between the HFA and OO groups.

Finally, on retrospective measures of head circumference growth, the rate of head growth followed by deceleration was greater in the OO and HFA groups than in the TD group, and not different from each other.

Results so far, therefore, indicate that cognitive and executive functioning in the OO group has really normalized, while the HFA group continue to show the expected executive deficits. Above average IQ may help the OO children to compensate. Early biological markers do not differentiate the OO from the HFA group, suggesting that any early structural or inflammatory process was not different for the OO than for other children with ASD. Psychiatric co-morbidity appears to persist in the OO children, perhaps suggesting that it represents an independent vulnerability and is not secondary to their autistic symptomatology.

101.04 Discussion.

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Moderator: E. Fombonne*McGill University*

102.00 Immunization Uptake in Siblings of Children with Autism. W. Roberts*[1], G. Abu Kuwaik[2], J. Brian[2], S. E. Bryson[3], B. MacKinnon Modi[2], I. M. Smith[3], P. Szatmari[4], N. Tanel[5] and L. Zwaigenbaum[6], (1)*University of Toronto*, (2)*Hospital for Sick Children & Bloorview Kids Rehab*, (3)*Dalhousie University/IWK Health Centre*, (4)*Offord Centre for Child Studies, McMaster University*, (5)*Hospital for Sick Children*, (6)*University of Alberta*

Background: Fears persist that vaccinations increase risk of autism spectrum disorders (ASD), despite epidemiological evidence to the contrary. Immunization rates have declined in many countries although data do not suggest risk. No one experiences these concerns more deeply than parents of children with ASD as they face the decision about whether to vaccinate younger siblings.
Objectives: To compare the immunization uptake of younger siblings of children with ASD to those of affected siblings and low-risk controls.
Methods: Participants included 160 younger siblings of children diagnosed with ASD ('high-risk siblings'), 91 of the affected older siblings ('probands'), and 56 low risk controls ('controls'; no family history of ASD). Data on immunization

status were obtained from medical records; specifically, the receipt/non-receipt and timing of administration of the Diphtheria, Pertussis, Tenanus and Polio (DPTP) and Measles, Mumps and Rubella (MMR) vaccines. Immunization was classified as 'incomplete' if a vaccine was not received, and as 'delayed' if a vaccine was received at least 3 months late relative to current Canadian guidelines (2, 4, 6, 18 months for DPTP; 12 months for MMR). Each participant was at least 18 months old at the time of data collection. Results: Of the high-risk siblings, 86 of 160 (53.8%) had records indicating delayed or incomplete immunization on either vaccine, in comparison to 20 of 91 probands with ASD (22%), and 5 of 56 low-risk controls (8.9%). Similar coverage rates were identified for DPTP and MMR vaccines in high-risk sibs (delayed or incomplete, respectively).

Conclusions: It appears that concerns regarding vaccinations and risk of ASD persist among families of children with ASD, as younger siblings have decreased and delayed uptake of vaccinations compared to older siblings and low-risk controls.

102.01 Examination of Mitochondrial Variation in Autism. J. L. McCauley*[1], M. Schmidt[1], S. H. Slifer[1], I. Konidari[1], P. L. Whitehead[1], W. Hulme[1], H. H. Wright[2], R. K. Abramson[2], D. J. Hedges[1], M. L. Cuccaro[1], J. R. Gilbert[1], J. P. Hussman[3], E. R. Martin[1], J. Haines[4] and M. A. Pericak-Vance[1], (1)*University of Miami Miller School of Medicine*, (2)*University of South Carolina School of Medicine*, (3)*Hussman Foundation*, (4)*Vanderbilt University*

Background: There has been increasing speculation that oxidative stress and abnormal energy metabolism may play a role in ASD (Autism Spectrum Disorders). It is essential that we begin to thoroughly identify and characterize the role of genes involved in oxidative stress, both those that reside in the mitochondria and those that are encoded in the nuclear genome. Of note there has been a profound lack of investigation into the role of mitochondrial variation in autism, despite numerous clinical reports describing patients with mitochondrial disorders or mutations who have symptoms consistent with ASD. Further, mitochondrial inheritance would be consistent with the observed increase in neuropsychological abnormalities in the mothers of ASD children.

Objectives: To comprehensively examine the role of mitochondrial variation and nuclear-encoded mitochondrial gene variation with regard to autistic risk.

Methods: We have resequenced a discovery dataset of ~200 Caucasian proband-father pairs (181 probands/185 fathers) using the Affymetrix Human Mito2.0 chip. We are examining haplogroups, characterizing both common and rare mitochondrial variations, and testing for association of both haplogroups and mitochondrial variation with ASDs. Additionally, we are utilizing genome-wide single nucleotide polymorphism data generated from the Illumina 1-M beadchip on all individuals to test for gene x gene interactions between mitochondrial variations and nuclear-encoded mitochondrial gene variations. A validation dataset of ~200 proband-father pairs is also being sequenced.

Results: A number of single-nucleotide polymorphisms (SNPs) within the nuclear-encoded genes demonstrate modest association in our recent GWAS study. We have initially examined European-Caucasian haplogroups and haplogroup defining single-nucleotide polymorphisms (SNPs) to assess the odds of carrying each mitochondrial haplogroup/ or haplogroup defining SNP in Autism probands compared to unaffected fathers. These preliminary results suggest that the A allele at mtDNA position 10398 is significantly (p= 0.007) overrepresented in autism probands compared to their unaffected fathers.

Conclusions: These data will yield insight into mitochondrial variation on a level never before performed in autism. Furthermore, this unique project will begin to examine the role oxidative stress genes may play in ASDs.

102.02 What Is a Meaningful Result? Communicating the Results of Genetic Research in Autism. F. A. Miller*, R. Z. Hayeems and J. P. Bytautas, *University of Toronto*

Background: Recent commentaries have argued that to honor the principles of respect for persons, beneficence and reciprocity, researchers bear an obligation to report genetic research findings to study participants (Shalowitz and Miller 2005, 2007, 2008; Ravitsky and Wilfond 2006; Fernandez et al 2003; Knoppers et al 2006). Clinical utility is regarded as a core criterion around which a judgment about disclosure should be made (Ravitsky and Wilfond 2006). Others contend that such clinical standards are far from clear and that ethical duties may neither be well

served if results are disclosed nor denied if they are not (Miller et al 2008).

Objectives: To contribute to this debate and inform policy and practice related to the communication of genetic research results to individual research participants, we sought to understand the experiences and beliefs of researchers engaged in genetics research in autism.

Methods: Researchers involved in studies designed to examine the genetics of autism spectrum disorders (ASD) were invited to participate in telephone or in-person semi-structured interviews about their beliefs, practices and expectations related to the research encounter and the putative obligation to report research results to study participants – specifically, genetic test results relevant to individual participants. Relevant respondents were identified in Canada, the US, the UK, and Europe through publicly available sources (i.e., academic publications, research group websites, etc.) and snowball sampling. Interview transcripts were analyzed qualitatively using constant comparison, reflexivity, and writing as an analytic device. In this analysis, we sought to better understand the nature of the meaning that researchers' assign to genetic research results.

Results: 23 researchers participated in this study. A first finding is that researchers are motivated to pursue their work, in part, by the perceived importance of understanding the causes of ASD; while recognizing that ASD is a complex, multi-factorial set of disorders, most believe that genetic factors are fundamental to their etiology. Second, most researchers believe that participants share their interest in understanding the causes of ASD, and further, believe that research findings that illuminate genetic causes would be valued by participants and warrant reporting. Despite this, researchers are not uniform in their views of what actually constitutes a 'meaningful result' in the context of ASD genetics research. Different evidentiary standards and theoretical assumptions are brought to bear in judging whether specific findings are meaningful enough to warrant reporting, including the relevance of a Mendelian logic, the co-existence of an expected phenotype, or a particular standard of molecular or statistical evidence. What is sufficiently meaningful to return to participants appears not only to be a function of attributes of the result itself, but also a function of other commitments and interests, including the opportunity that a given result presents to pursue additional research.

Conclusions: If clinical utility is to remain the standard that governs the return of genetic research results to study participants, itself an open question, our data suggest that what constitutes a 'meaningful result', and by extension, clinical utility - in the context of ASD - is far from resolved.

102.03 Efficacy and Safety of Aripiprazole for the Treatment of Irritability Associated with Autistic Disorder in Children and Adolescents (6–17 Years): Results from Two 8-Week, Randomized, Double-Blind, Placebo-Controlled Trials. R. Owen[1], R. Melmed*[2], L. Laird[1], G. Manos[1], W. H. Carson[3] and R. D. McQuade[3], (1)*Bristol-Myers Squibb*, (2)*Director, Melmed Center*, (3)*Otsuka Pharmaceutical Development and Commercialization Inc.*

Background: Many individuals with autistic disorder also experience problematic behaviors including irritability, aggression, tantrums, rapidly changing moods, and self-injurious behavior. Atypical antipsychotics may be useful for the treatment of these behaviors in the context of a comprehensive treatment program.

Objectives: Evaluate the short-term efficacy and safety of aripiprazole in the treatment of irritability associated with autistic disorder

Methods: Two 8-week, randomized, double-blind, parallel-group trials evaluated the efficacy of aripiprazole (flexible dose [2–15 mg] and fixed dose [5, 10 and 15 mg/day]) versus placebo using the caregiver-rated Aberrant Behavior Checklist Irritability Subscale (ABC-I, which measures symptoms of aggression, tantrums, and self-injurious behavior) as the primary endpoint. Secondary efficacy measures, as well as safety and tolerability, were also assessed.

Results: Ninety-eight patients were randomized in the flexible dose trial, 218 patients in the fixed dose trial. Statistically significant greater improvement was seen with aripiprazole in both trials on the ABC-I at endpoint (Week 8 [LOCF] $p<0.05$). Secondary results favoring aripiprazole over placebo ($p\leq0.05$ at endpoint [LOCF]) included the Clinical Global Impression – Improvement and the ABC Hyperactivity and Stereotypy Subscales (2–15; 5, 10, 15 mg); Clinical Global Impression – Severity of Illness (2–

15; 10, 15 mg only); Children's Yale-Brown Obsessive Compulsive Scale (modified), Inappropriate Speech Subscale (2–15; 15 mg only); and Response Rate (2–15mg; 5 mg only). Discontinuation rates due to adverse events (AEs) were: flexible dose: placebo 6%, aripiprazole 11%; fixed dose: placebo 8%, aripiprazole – 5 mg 9%, 10 mg 14%, and 15 mg 7%. Adverse events (sedation, drooling, tremor, fatigue) were similar between the trials. There were two serious AEs: presyncope (5 mg) and aggression (10 mg) in the fixed dose trial. Mean weight gain at week 8 ($p<0.05$ for each vs. placebo) was – flexible dose 1.9 kg (2–15 mg) and 0.5 kg (placebo) and fixed dose 1.5 kg (5 mg), 1.4 kg (10 mg), 1.6 kg (15 mg), and 0.4 kg (placebo).

Conclusions: Aripiprazole was efficacious in the treatment of irritability in children and adolescents with autistic disorder and was generally safe and well-tolerated in two short-term trials, although significant weight gain was observed in some subjects.

102.04 Moderators and Mediators of Risperidone Response in Autistic Disorder with Irritability. C. A. Farmer*[1], L. E. Arnold[1], A. N. Witwer[1], R. Disilvestro[1], M. G. Aman[1], J. McCracken[2], C. McDougle[3], L. Scahill[4], E. Tierney[5], B. Vitiello[6] and R. U. P. P. Autism Network[7], (1)*Ohio State University*, (2)*University of California, Los Angeles*, (3)*Indiana University School of Medicine*, (4)*Yale University School of Medicine*, (5)*Kennedy Krieger Institute*, (6)*National Institute of Mental Health, National Institutes of Health*, (7)*Research Units on Pediatric Psychopharmacology Autism Network*

Background: The NIMH Research Units on Pediatric Psychopharmacology (RUPP) Autism Network reported an 8-week double-blind comparison of risperidone (N = 49) to placebo (N = 52) in children and adolescents age 5-17 (mean 8.8 years) (RUPP Autism Network, 2002). Intention-to-treat (ITT) analyses showed risperidone had highly significant effects on the main outcome measure, the Irritability subscale of the Aberrant Behavior Checklist (ABC; Aman et al., 1985), with a 57% decrease versus a 14% decrease in placebo (d = 1.2).

Objectives: This report explores potential moderators and mediators of the effects of risperidone on the main outcome measure. Demographic data (e.g., parent income), ratings on other instruments (e.g., ABC Hyperactivity), medication adherence, and biological data (e.g., leptin levels) were all explored in the analysis.

Methods: Potential moderators and mediators were entered (continuous form where possible) into the original ITT analysis. The MacArthur Foundation Network subgroup (Kraemer et al., 2001, 2002) guidelines for moderation and mediation were employed. As partial correction for numerous comparisons, significance was set at p = 0.01.

Results: Initial severity of ABC Irritability was the only significant moderator of response to risperidone (χ^2 = 15.09, p = 0.0001). CeruloplasminRID, a measure of copper, was marginally significant (χ^2 = 4.87, p = 0.027). Medication adherence, optimal dose, and weight gain (percent) were significant mediators of response (χ^2=7.39, p = 0.0066; χ^2=8.19, p = 0.0042; and χ^2=19.34, p = 0.0001, respectively). Weight gain appeared to predict improvement better with placebo than active drug. A number of baseline variables (e.g., parent income and education, CGI Severity) were nonspecific predictors, having a significant main effect on outcome, but not a significant triple interaction with time and treatment. Percent change in serum 5'nucleotidase, a zinc marker, had an effect on outcome that was moderated by risperidone [i.e., significant triple interaction with time and treatment (χ^2=17.35, p < 0.0001), but not correlated with treatment].

Conclusions: Overall, the paucity of moderators and mediators of risperidone response may be scientifically disappointing but is clinically encouraging; it indicates that risperidone is appropriate for a wide range of children with autism and disruptive behaviors. The relation of high initial severity to greater change is not surprising, and is undoubtedly at least partly regression to the mean, possibly enhanced by treatment. Medication adherence is commonly shown to mediate response to various treatments, and this finding emphasized its role in treatment efficacy. The mediation by dose, although statistically significant, may be an artifact of titration; it was consistent with a physician prescribing increasing doses of placebo in the face of unimproved behavior and no side effects. Perhaps the most important result was that weight gain predicted response in both groups, and seemed to be a somewhat better predictor for placebo than risperidone. This implies that it might be difficult to separate the benefits of weight gain from the benefit of risperidone. Drug

moderation of the effect of 5'nucleotidase change was robust enough to survive severe Bonferroni correction and seems worthy of further study, which is required before conclusions are warranted.

102.05 Poor Verbal and Non-Verbal Skills in Children with Abnormal Craniofacial Variability Indices (CVI) and ASD. K. Angkustsiri*[1], K. Camilleri[2], L. Cochran[2], C. W. Nordahl[2], L. A. Barnett[2], R. L. Hansen[2], A. M. Mastergeorge[2], S. J. Rogers[2] and S. Boyadjiev Boyd[1], (1)*University of California at Davis*, (2)*M.I.N.D. Institute, University of California at Davis*

Background: Physical phenotyping of children with ASD often relies on subjective assessment, as direct measurement of young children is difficult. Three-dimensional photometry allows objective capture of images quickly and reliably to obtain multiple indirect anthropometric measurements. Prior studies in older children and adults with ASD show poorer cognitive and verbal abilities in those subjectively rated as having abnormal physical features (Miles, et al. 2005). This analysis characterizes the verbal and non-verbal functioning of young children with abnormal physical features determined from objective measurements obtained through 3D-photometry.

Objectives: To subgroup children with ASD into those with normal and abnormal Craniofacial Variability Indices (CVI is a composite measure representing facial proportion) and compare groups in terms of verbal and non-verbal abilities using standardized measures.

Methods : Children ages 2-5 years participated in the Autism Phenome Project, a longitudinal study aimed to biomedically and behaviorally phenotype ASD. Images from 28 Caucasian males were landmarked, and at least 9 facial measurements were compared to published norms to determine z-scores for each measurement. CVI was calculated as each individual's standard deviation of all z-scores, with a value >1.2 considered atypical (~95th percentile in a normal population (Garn, et al. 1985). CVI therefore provides quantitative description of departure from the norm. A diagnosis of ASD was confirmed with the ADI-R and the ADOS. Standard scores within 1 SD on the PPVT-IIIA and EOWPVT defined "average" language level, and "low" language level included scores >1 SD from the mean. Developmental ratios (mental age/chronologic age) were calculated from subtests of the MSEL for verbal and non-verbal abilities. Scores were not normally distributed and sample size was small, so the Wilcoxon Mann-Whitney test was used unless specified.

Results: Children with "low" language levels had statistically significantly higher mean CVI (0.94;SD 0.2 vs. 0.73; SD 0.14) than children with "average" language levels (p=0.04). Two of the 28 boys had abnormal CVI >1.2. Both (100%) boys with abnormal CVI were in the "low" language level compared to 81% (21/26) of children with CVI<1.2 (x^2; p=0.5). Mean verbal ratios were lower for those with abnormal CVI, (0.44;SD 0.25 vs. 0.63;SD 0.13) although this did not reach statistical significance (p=0.3). Mean non-verbal ratios were lower (0.52;SD 0.19 vs. 0.71;SD 0.08), with a trend toward statistical significance (p=0.07). ADOS scores were higher for this group (19;SD 1.41 vs. 13.8;SD 4.5), but this was not statistically significant (p=0.16). Conclusions: Our data suggest that children with abnormal CVI perform more poorly on verbal and non-verbal measures and have higher ADOS scores, although this did not reach statistical significance, likely due to the small sample size. This supports earlier studies that used the presence of atypical physical features as a marker for poorer cognitive and verbal abilities and identifies similar patterns in a younger population based on objective quantitative measures. Additional subjects are needed to increase statistical power. It is possible that the abnormal CVI may be used as a predictor for poor verbal and non-verbal skills. Such patients may benefit from more thorough genetic evaluation and testing.

Conclusions:

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103.00 Lateral Masking Paradigms Reveal Atypical Interactions in Autism. L. Kéïta*, V. Fay, L. Mottron and A. Bertone, *Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*

Background: Bertone et al. (2005) demonstrated that autistics were superior to nonautistics in identifying the orientation of static gratings consisting of simple, luminance-defined information. However, autistics were inferior when the gratings consisted of complex, texture-defined information. These authors suggested that the

most biologically plausible type of neural alteration congruous with this dichotomous performance was strong or enhanced lateral inhibition, a type of lateral connectivity within the primary visual cortex that mediates the extraction of low-level static information.

Objectives: This study aimed at assessing the hypothesis of atypical lateral connectivity in autism using lateral masking paradigms (Polat & Sagi, 1993). In such paradigms, the sensitivity of a centrally presented Gabor target stimulus is affected by lateral (or flanking) stimuli presented simultaneously at certain distances from the target. This lateral interaction is dependent on different variables, including target/flanker distance (Polat & Sagi, 1993) and the contrast of the flanking stimuli (Yu et al., 2002).

Methods: 10 autistic and nonautistic participants matched for chronological age (mean of 22 years), full-scale IQ, gender and handedness completed the experimental tasks. Detection thresholds for vertically oriented target Gabor stimuli were measured alone (no flanker condition), and with same-orientation flanking stimuli presented above and below at two different distances (3 and 6 lambda). In an additional condition, the distance between the target and flankers was set at 3 lambda; the contrast of the flankers (presented orthogonal to the target) was varied from 0.05, 0.1, 0.2, 0.4 and 1. Target detection thresholds in both conditions were measured using an adaptive staircase procedure.

Results: As expected, both groups showed facilitation at 3 lambda (increased sensitivity to target) in Experiment 1. However, a relatively greater facilitation was demonstrated by the autistic participants. No between-group difference was found for the 6 lambda condition. Manipulating the contrast of the flankers did not result in between-group differences.

Conclusions: The findings from this study represent behavioral evidence for atypical lateral connectivity (i.e. excessive lateral inhibition) mediating spatial information processing within early visual areas in autism. It is suggested that the behavioral consequence of this neural hypothesis (either enhanced or diminished sensitivity to static stimuli), is dependent upon the physical attributes defining the information being analyzed (Vandenbroucke et al., 2008).

103.01 Enhanced Mental Rotation Abilities in Autistic Individuals. I. Soulieres*[1], T. A. Zeffiro[2], J. Lepage-Hamel[1], M. L. Girard[1] and L. Mottron[1], (1)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (2)*Neural Systems Group, Massachussetts General Hospital*

Background: Autistic strengths in low-level perception and visuospatial skills are being increasingly recognized. For example, it is well established that autistics excel at the Block Design task. Visual imagery, the formation and manipulation of mental images, represents a key ability for successfully solving visuospatial problems like the Block Design task. Mental rotation consists in deciding whether two shapes are identical or different (mirror-reversed) after mentally rotating one shape to the position of the other shape. Autistic individuals are reported to be faster than nonautistic individuals at mental rotation involving three-dimensional geometric shapes (Falter et al., 2008), and to exhibit less task-related activity in frontal cortex (Silk et al., 2006).

Objectives: This study first explored mental rotation with different task material types to test the robustness and scope of the reported group differences in visual imagery. Second, it aimed to characterize the mechanisms responsible for these differences by asking: a) Is the difference linked to visual imagery or more generally to the processing speed of perceptual information?, and b) Does the difference lie in the capacity to form a mental representation of the objects or to "spatially manipulate" that representation?

Methods: Participants were 14 autistic and 14 nonautistic individuals, matched on age (mean 21 years), sex, manual preference and Wechsler IQ (mean 104). We used four mental rotation same-different tasks, including images of two-dimensional geometric figures, three-dimensional geometric figures, drawings of hands and letters. We investigated the second aim by comparing performance in mental rotation with: a) speed of perceptual processing and b) visual imagery without manipulation of the mental representation. Speed of perceptual processing was measured using a classic inspection time task, in which participants indicated which of two very briefly presented vertical lines was longer. A staircase procedure was used to estimate the minimal exposure time for each participant. For the visual imagery task, participants imagined a

specified letter in a circle and then decided which of two highlighted portions of the circle would contain the greater proportion of the letter.

Results: Mixed effects linear models were used for the four mental rotation tasks. The analysis showed a significant between-group difference in accuracy intercept for hand stimuli, and in both accuracy and response time for letters. In both cases, autistic participants had faster or more accurate performance. There were no significant between-group differences in the mental rotation of 2D and 3D figures, although trends were seen in the same direction. The visual imagery and inspection time tasks yielded no significant between-group differences.

Conclusions: Subtle but consistent increased performance in mental rotation with various materials was found in autistic individuals. As the processing speed of perceptual information and ability to form mental representations did not differ between groups, the different performance in mental rotation is therefore likely to arise from a differing ability to spatially *manipulate* the mental representations of objects. This ability could be beneficial in various complex cognitive tasks such as matrix reasoning or drawing and interpreting plans, and might be exploited in educative methods with autistic individuals.

103.02 Assessing Lateral Connectivity in Autism Using a Crowding Paradigm. A. Bertone*[1], V. Fay[1], J. Faubert[2], L. Kéïta[1] and L. Mottron[1], (1)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (2)*Université de Montréal*

Background: Crowding, often defined as the deleterious influence of nearby contours on visual discrimination, is a form of inhibitory interaction and is ubiquitous in spatial vision (i.e., Levi et al., 2008). Generally, the ability to discriminate a target stimulus is more difficult when distractors (or flanking stimuli) are simultaneously present within a proximal spatial zone of interaction. For example, the ability to discriminate the orientation of a Landolt C optotype is maximally degraded when the bars are simultaneously presented within a certain distance of the C, referred to as the *critical distance*. The most congruent physiological explanation for this effect implicates lateral connections (both excitatory and inhibitory) between orientation-specific neurons in low-level visual areas (i.e., V1).

Objectives: To assess lateral connectivity mediating low-level spatial information processing in autism by measuring the far visual acuity of a Landolt-C optotype alone, and with flanking stimuli presented at different distances from the target.

Methods: Ten autistic and nonautistic participants matched for chronological age (mean of 22 years), full-scale IQ, gender and handedness were asked to identify the gap-opening orientation of high-contrast Landolt-C stimuli. The gaps in the C-optotypes were presented at either left, right, top or bottom positions. Five different conditions were assessed; C-optotypes were presented without flanking bars (far visual acuity condition), or with four flanking bars (crowding conditions) placed either abutting the optotype, or at a distance of one, two, and three gap-opening widths from the C-optotype. Flanking bar sizes and distances were always proportional to the size of the C-optotype (one gap width across and 5 gaps width in height), positioned to the left, right, above and below the target (Flom et al.,1963). Far visual acuity, defined as the minimal C optotype size needed to correctly identify gap-opening orientation, was tested for each condition using an adaptive staircase procedure.

Results: Contrary to recent findings (Ashwin et al., 2008), no significant between-group differences in visual acuity were found for the no flanker condition. As expected, crowding decreased visual acuity for both autistic and nonautistic groups. However, whereas the critical distance (flanker distance most affecting acuity) for the nonautistic participants peaked at the one gap-opening width, autistic far visual acuity was affected at all gap widths, albeit to a lesser extent. The largest between-group difference was found at 3 gap widths where no flanker effect on acuity was evident for the nonautistic group, whereas crowding decreased visual acuity for the autism group.

Conclusions: The present study demonstrates that although autistic participants present visual acuity comparable to nonautistic individuals, autistic acuity is differentially affected by crowding when assessed near the acuity limit. We suggest that these results are consistent with atypical lateral connectivity within early visual areas in autism, particularly within the context of spatial information processing. Results will be discussed

within the context of current theories suggesting a low-level origin for atypical visual information processing in autism.

103.03 Attention Regulation and Social Behavior among Higher Functioning Children with Autism. L. Mohapatra[1], H. A. Henderson*[1], C. Schwartz[2], N. Kojkowski[1], C. Hileman[1], K. E. Ono[1] and P. C. Mundy[3], (1)*University of Miami*, (2)*Yale University*, (3)*UC Davis*

Background: Attention regulation and cognitive control are core components of self-regulation and are required for effective social interactions among both typically developing children and children with autism. Studies of the neurophysiological (ERP) correlates of cognitive (N2) and attention control (P3) demonstrate both developmental change and individual differences across childhood and adolescence.

Objectives: The goal of the current study was to examine N2 and P3 responses during a cognitive control task in a sample of children with higher functioning autism (HFA) and a matched sample of typically developing children. We were particularly interested in the associations between N2 and P3 amplitudes and measures of symptom severity, emotional wellbeing, and social competence and whether these associations differed across diagnostic groups.

Methods: Data are reported on a preliminary sample of 55 children (28 HFA, 27 comparison) between 8- and 16-years of age. EEG was collected continuously as children completed a modified version of the Eriksen Flanker Task. N2 amplitude was measured as the most negative peak at frontal sites (Fz, FCz) between 250-400 ms after incompatible stimulus onset and P3 amplitude was measured at the most positive peak at frontal sites located 300-600 ms after incompatible stimulus onset. Dependent variables included the total score from the Social Communication Questionnaire (SCQ), *Internalizing Problems,* assessed using the parent report of the Behavior Assessment System for Children, *Personal Adjustment*, assessed using the child self-report version of the BASC-2, and *Reciprocal Social Interactions,* assessed in the laboratory as each child interacted with an unfamiliar peer. In contrast, for children in the comparison sample, smaller N2 amplitudes were associated with fewer Internalizing Problems and more Reciprocal Interactions, whereas P3 amplitude was less strongly associated.

Results: Preliminary results indicate that children with HFA did not differ from comparison children in N2, t (1, 53) = -.44, *ns*, or P3, t (1, 53) = 1.70, *ns*, amplitude. A series of regression analyses were conducted with each of the dependent measures regressed on (1) Diagnostic Group, (2) N2 and P3 amplitude, (3) the interaction of N2 and P3 amplitude with Diagnostic Group. In summary, the ERP measures differentially predicted symptom severity and social outcomes depending on diagnostic group. Specifically, for children with HFA, larger amplitude N2 and P3 responses predicted less severe symptomatology, fewer Internalizing Problems, and more Reciprocal Social Interactions, and larger P3 responses predicted better Personal Adjustment.

Conclusions: Individual differences in ERP responses within each diagnostic group predicted variation in symptom severity, emotional wellbeing, and social competence. Smaller N2s were associated with better outcomes for children in the comparison sample, which is consistent with prior work suggesting that by late childhood smaller N2 responses index better cognitive control. However for HFA children larger N2 and P3 responses predicted better functioning suggesting that more effortful cognitive and attention control may benefit children who by definition have impaired social and communicative functioning. These results will be discussed in the context of potential differences in the developmental neurophysiology of self-regulation between typically developing children and children with autism.

103.04 The Development of Cognitive Control in Children with Autism Spectrum Disorders. S. Ly, M. Solomon*, J. H. Yoon and C. S. Carter, *MIND Institute, Imaging Research Center*

Background: Individuals with autism spectrum disorders (ASDs) exhibit impairments in cognitive control which are associated with atypicalities in the dorsolateral prefrontal (DLPFC), anterior prefrontal (aPFC), anterior cingulate (ACC), and parietal cortices. As yet, there has been little study of the developmental trajectory of the neural correlates of cognitive control in ASDs.

Objectives: To investigate the developmental trajectory of cognitive control in adolescents and young adults with ASDs and typical development; to examine changes in functional connectivity with age; and to test whether network and other measures are related to symptoms of inflexible thoughts and/or behaviors, and attention deficits.

Methods: Participants included 4 groups of 15 individuals with ASDs and typical development

(TYP) each divided into younger (ages 12-15) and older (ages 16-18) groups. Slow event-related functional magnetic resonance imaging (fMRI) was used to examine group differences in performance in the cue phase of the Preparing to Overcome Prepotency (POP) task, which is a stimulus response incompatibility paradigm. Beta series correlations between brain regions activated during previous studies of cognitive control, were used as seed regions in the investigation of age-relatd changes in functional connectivity between regions including anterior PFC (aPFC) and DLPFC in a multivariate method based on graph-theory and adapted from Dosenbach, Fair, Cohen, Schlaggar and Petersen (2008). A second multivariate "small world network- based" developmental connectivity analysis, adapted from Achard, Whitcher, Suckling, and Bullmore (2006), also was implemented in a whole brain analysis.

Results: Across both groups and methods, younger individuals exhibited higher levels of brain activation in frontal and parietal regions than older ones. Using the graph-theory approach, the ASD group showed a pattern of "catching up" to the TYPs. For example, the TYP group exhibited increased network integration over time between regions of the aPFC, the DLPFC, and the occipital cortex. In the young TYPs, aPFC connections were limited; however, integration with occipital cortex became evident for the older age group. For the DLPFC, younger TYPs exhibited connectivity with aPFC, thalamus and temporal parietal junction. Older TYP children did not exhibit prominent DLPFC connectivity during the task. For the young ASD group, connectivity with aPFC and DLPFC was limited, however, by the older group ASD group demonstrated patterns of regional connectivity comparable to younger TYPs. Small-world network analysis implemented for the whole brain, showed a similar pattern of findings related to overall network changes in both groups with development, and with deficits in fronto-parietal connectivity in the ASD group at both ages. TYPs also showed greater long-range connectivity, and better network integrity than ASDs. A measure of network integrity was significantly related to restricted and repetitive behaviors in the ASDs group.

Conclusions: Results suggest that ASDs involve developmental delay in connectivity in the aPFC and DLPFC and a general deficit in parietal connectivity. They also show that ASDs exhibit reduced long-range connectivity across both regions, and provide preliminay support for the hypothesis that individuals with ASDs "catch up" to TYPs with respect to the activation patterns found in neural networks during control tasks.

103.05 Neuropsychological Functioning in First-Degree Relatives of Individuals with Autism. L. D. Stanford*, M. W. Mosconi, A. M. D'Cruz, L. Ankeny, M. Kay and J. A. Sweeney, *University of Illinois at Chicago*

Background: Unaffected first-degree relatives of individuals with autism show cognitive deficits that parallel impairments observed in probands with autism. A comprehensive evaluation of neuropsychological domains in family members is needed to identify cognitive endophenotypes that reflect subtle neural system dysfunction that might be genetically determined.

Objectives: To examine neuropsychological functioning across multiple domains in unaffected first-degree relatives of individuals with autism.

Methods: Sixty-two first-degree relatives of individuals with autism and 31 age- and IQ-matched healthy control individuals between 8-55 years of age completed a neuropsychological battery spanning five domains: social functioning, communication, executive functioning, motor ability, and memory. For the social-emotional domain, the Penn Emotion Differentiation Task and Social scale of the Autism Symptom Quotient (ASQ) were administered. For the communication domain, the Peabody Picture Vocabulary Test – Third Edition (PPVT-III) and Communication scale of the ASQ were used. Executive function measures included Spatial Span from the Wechsler Memory Scale-III (WMS-III), Trail-Making Test B, and Digit Span from the age appropriate Wechsler Intelligence Scale. Motor tasks included the Grooved Pegboard Test and Finger Tapping Test. Memory tests included both the Faces and Word Lists subtests from the WMS-III or Children's Memory Scale (CMS). Mean Z-scores were calculated across subtests within a given domain. Individual tests also were examined.

Results: Family members showed worse performance than controls for the social-emotional and executive function domains, but no differences were observed for communication, motor, or memory domains. Family members were slower to identify facial emotions, showed

more social abnormalities on the ASQ, scored lower on Spatial Span and Digit Span, were slower to complete Trails B, and had greater difficulty shifting their attention as measured on the ASQ. Family members also performed worse on the communication scale of the ASQ. For family members, scores on the social, communication and attention switching scales of the ASQ were correlated. Performance on the social scale also was associated with performance on Spatial Span, the latter of which was also significantly related to performance on Trails B. For controls, only scores on social and communication scales of the ASQ were correlated. Ratings on the social scale were correlated with Digit Span, and Trails B performance was associated with both Digit Span and Spatial Span. Family members showed greater within-group variability on measures of executive functioning.

Conclusions: First-degree relatives of individuals with autism show poorer performance on measures of social-emotional functioning, communication, and executive processing. These lower performance patterns parallel the core features of autism. Still, while reduced to a statistically significant degree, family members' performance on all domains was in the average range and, for measures of executive functioning, was characterized by greater within group variability than is seen in controls. In contrast, family members did not show performance deficits on tasks of motor, memory, or simple language functioning suggesting that a specific profile of neurocognitive performance characterizes relatives of individuals with autism better than a general intelligence factor. This pattern may offer clues for selecting endophenotypes for family genetic research.

Oral Presentations Program
104 Molecular Genetics I

104.00 A Genome-Wide Association Study of Autism Reveals a Common Novel Risk Locus at 5p14.1. D. Q. Ma*[1], D. Salyakina[1], J. M. Jaworski[1], I. Konidari[1], P. L. Whitehead[1], S. H. Slifer[1], D. J. Hedges[1], H. N. Cukier[1], J. L. McCauley[1], G. W. Beecham[1], H. H. Wright[2], R. K. Abramson[2], E. R. Martin[1], J. P. Hussman[3], J. R. Gilbert[1], M. L. Cuccaro[1], J. Haines[4] and M. A. Pericak-Vance[1], (1)*University of Miami Miller School of Medicine*, (2)*University of South Carolina School of Medicine*, (3)*Hussman Foundation*, (4)*Vanderbilt University*

Background: Autism is one of the most heritable neuropsychiatric disorders. However, its underlying genetic architecture has largely eluded description.

Objectives: To comprehensively examine the hypothesis that common variation is important in autism

Methods: We performed a genome-wide association study (GWAS) using a discovery dataset of 438 autistic Caucasian families genotyped on the Illumina Human 1M beadchip and validated the results using a publicly available GWAS dataset genotyped on 487 Caucasian autism families using the 550K Illumina beadchip.

Results: 96 single nucleotide polymorphisms (SNPs) demonstrated strong association with autism risk (p-value < 0.0001). 62 out of the top 96 SNPs were genotyped in the validation dataset. A novel region on chromosome 5p14.1 (25,830-26,100kb) appeared to be the only region being validated with a cluster of 3 SNPs (p [0.01, 0.04]). This encouraged us to have a closer investigation into this region. A further joint analysis of 46 SNPs genotyped on both datasets identified over 9 SNPs having more significant p-values (0.002 to 4.17E-6) than in either dataset alone. The examination in this region shows numerous sequence segments exhibiting a high degree of evolutionary conservation. In addition, there are three CNVs in proximity of the most significant SNPs. Although the immediate 1 Mb vicinity of the association region contains no known genes or candidates, flanking the region are CDH9 and CDH10, two genes that belong to the cadherin family, a group of proteins containing members that are involved in calcium-dependent cell-cell junctions in the nervous system and possible targets of regulatory action. The exhaustive molecular analysis is ongoing (see Griswold et al., this meeting).

Conclusions: Our findings demonstrate that in addition to multiple rare variations, part of the complex genetic architecture of autism involves common variation.

104.01 Autism Genome Project. J. Sutcliffe for the Autism Genome Project*, *Vanderbilt University*

Background: Autism is a neurodevelopmental disorder that affects approximately 1 in 150 individuals and is characterized by deficits in reciprocal social interaction, communication and patterns of repetitive behaviors and restricted interests. Twin and family studies indicate high

heritability, but evidence supports a highly complex architecture for the underlying genetic etiology. The Autism Genome Project (AGP) was formed to facilitate gene identification by uniting investigators and family data. AGP Phase I involved genome-wide (GW) analysis of linkage and copy number variation (CNV) in >1100 multiplex families. Linkage analysis revealed promising loci on 11p and 15q, with gender and ancestry influencing signals at these and other loci. Copy number analysis of 10k data showed a striking degree of CNV, with instances of both inherited and de novo CNV. Objectives: AGP Phase II involves GW analysis for association and copy number variation using the Illumina 1M SNP array in a dataset to ultimately reach ~3,000 families. We have completed analysis for an sample of ~1,500 parent-child trios for association and CNV, and combined analyses include data from >700 AGRE families genotyped for the 550k subset of markers (~2,200 families total). Thus, the AGP represents by far the largest genetic study undertaken for autism. Methods: Raw 1M SNP data was distributed for CNV analysis, while genotypes were assessed for quality control (QC), ancestry and Hardy-Weinberg equilibrium (HWE) prior to analysis for association. Results: In copy number analysis, multiple algorithms were utilized to infer CNV from intensity and genotype data, and ~59,889 CNVs were called by at least two algorithms. Mean and median CNV sizes were 95kb and 42kb, respectively, and 20 CNVs were detected per proband on average. Numerous de novo and inherited variants were identified in novel loci highlighting previously implicated pathways (e.g. neuronal cell adhesion molecules) and conditions with overlapping genetic etiologies (e.g. mental retardation, schizophrenia). Family-based association analysis of ~1,500 AGP families using 1M data alone, or combined with AGRE families, does not reach GW-significance, and this highlights the underlying genetic heterogeneity of autism and what are certain to be small effect sizes. Of SNPs with $10\text{-}4 < P < 10\text{-}7$, numerous identify genes related to neuronal development and guidance, similar to those identified by CNV. Integration of CNV and association results is underway to prioritize follow-up studies. Replication of association findings in the next stage of the AGP will be important for their ultimate interpretation. Conclusions: We conclude from these data that collectively rare variation, particularly from CNV, contributes substantially to autism risk or causation. If, as seen in studies of type 2 diabetes, common allele effect sizes correspond to odds ratios of (e.g.) 1.2-1.3, much larger samples will be required in order to provide sufficient power for risk allele identification.

104.02 Novel Copy Number Variants in Children with Autism and Additional Developmental Anomalies. L. Davis*, K. Meyer, D. Rudd, A. Librant, E. Epping, V. Sheffield and T. Wassink, *University of Iowa*

Background: The etiology of autism appears to be primarily genetic, with karyotypically detectable chromosomal abnormalities accounting for ~5-7% of autism spectrum disorder cases. The emergence of DNA microarray technology has enabled detection of submicroscopic deletions and duplications that are referred to as copy number variants (CNVs) and are operationally defined as insertions or deletions larger than 1 kb. Recent studies have suggested a role for CNVs, both de novo and inherited, in the etiology of autism. Objectives: We hypothesized that children with autism and additional developmental abnormalities may be more likely to harbor novel CNVs whether de novo or inherited. We used this model for two reasons: 1) children with chromosomal abnormalities often have multiple or syndromic developmental anomalies and 2) we recently reported a pathogenic microdeletion in a child with autism and structural eye abnormalities, stimulating our interest in investigating other individuals with autism and additional developmental disturbances. Methods: We used Affymetrix 250K GeneChip Microarray technology to detect CNVs in a subset of children from the Autism Genetic Resource Exchange (AGRE). We selected children with autism who had additional phenotypic features suggestive of a developmental disturbance (positive criteria filter) but who had normal cytogenetic testing (negative criteria filter). We identified 17 families (typically excluded from genetic studies because of these additional phenotypes) with the following features: two or more children with autism, at least one of whom also had cranio-facial dysmorphology, limb or digit abnormalities, or ocular abnormalities. We also analyzed a group of 19 unrelated children with autism and no additional dysmorphology to compare numbers of novel CNVs between syndromic autism and non-syndromic autism. We also screened a sample of 716 unselected controls from a study of age related eye disorders ongoing at the University of Iowa. To detect changes in copy number we used a publicly available program, Copy Number

Analyser for GeneChip® (CNAG) Ver. 2.0. The CNVs of interest were validated using quantitative PCR. Results: A fisher's exact test of the number of novel CNVs out of the total number of CNVs in each group yields a one-tailed p-value of .04, suggesting that there are significantly more novel CNVs in the sample of syndromic autism. However, the number of individual carriers of novel CNVs did not differ significantly between the groups as there were two individuals in the syndromic autism group who each carried two novel CNVs. We identified novel deletions and duplications on chromosomes 1q24.2, 3p26.1, 4q34.2, 6q24.3, 7q35 and 22q11.2. Conclusions: Several of these deletions and duplications include new and compelling candidate genes for autism such as syntaxin binding protein 5 (STXBP5 also known as tomosyn), CNTNAP2 and leucine rich repeat neuronal 1 (LRRN1 also known as NLRR1). The implications of these novel and potentially pathogenic CNVs will be discussed as well as the psychiatric phenotypes found in the transmitting parents. Lastly, our data suggest that rare microdeletions and duplications may have a substantially higher prevalence in children with autism plus additional developmental anomalies.

104.03 Exon-Focused Microarray Analysis of Candidate Genes in Autism. M. Shinawi*[1], T. Sahoo[1], P. B. Santos-Celestino[1], R. Zascavage[1], J. R. German[1], A. Porter[1], P. Fang[1], D. E. Treadwell-Deering[2], C. Skinner[3], S. A. Skinner[3], R. E. Stevenson[3], R. P. Goin-Kochel[1] and A. Beaudet[1], (1)*Baylor College of Medicine*, (2)*Texas Children's Hosptial, Baylor College of Medicine*, (3)*Greenwood Genetic Center*

Background: We are pursuing two hypotheses, first that de novo and recent mutations cause a major fraction of autism cases, and second that a different fraction of autism cases may be caused by epigenetic mutations (see Person et al. epigenetic abstract). Neither de novo genetic mutations nor epigenetic mutations (epimutations) would be detected by genome-wide linkage studies. The high heritability of autism as judged by high concordance in monozygotic (MZ) twins and the low concordance in dizygotic (DZ) twins is precisely what would be expected for an etiology based on de novo mutations and could fit as well for de novo epimutations occurring prior to MZ twinning. Much progress in understanding the etiology of autism is derived from the use of array technologies to detect genomic deletions and duplications followed by sequencing of candidate genes within these genomic regions. Objectives: The goal of this work is to discover novel genomic deletions and duplications causing autism with a particular focus on determination of exon copy number to identify small deletions that would implicate a single protein coding gene. Genes suspected of causing autism via haploinsufficiency would then be sequenced in other autism individuals. Methods: Customized Agilent arrays were designed to cover all the exons of tens to hundreds of autism candidate genes. Genes were selected based on literature support that they might cause autism (73 genes), on neurological or synaptic function (253 genes), or on an implied role in epigenetic regulation (~300 genes). A one-million oligonucleotide array to test copy number for all exons in the genome is in development. Further characterization of the pathogenic variations was performed utilizing the Agilent 244K Whole Human Genome CGH array. The study group included 98 patients from South Carolina Autism Project, 64 local patients, and 22 autistic individuals from AGRE collection. Results: These experiments identified several very small and apparently benign copy number variants (CNVs) within the NRXN3, CACNAIC, GIRK2, and many other genes. Multiple lymphoblast cell lines were trisomic for various chromosomes, three for chromosome 12, one for chromosomes 9 and 12, and one for chromosomes 9 and 14. These were interpreted to represent cell culture artifacts. We found 5 cases with pathogenic alterations. Two of these abnormalities were deletions: a 15q13.3 deletion encompassing the CHRNA7 gene and a paternally inherited 2-Mb deletion causing haploinsuffiency of the BDNF and LIN7C genes. In addition, there were three different duplications involving X-linked genes and the 15q11-q13 imprinted domain. The X-linked duplications were detected in males and included a maternally inherited 615-kb duplication encompassing the OCRL1 gene and a de novo duplication of the SYBL1 gene. Conclusions: These data provide additional support for the importance of copy number variants in the etiology of autism and suggest that exon-focused microarrays may be an effective method for detecting these chromosomal imbalances and identifying specific causative genes. The utilization of arrays that cover all exons in the genome is predicted to increase the detection of these chromosomal imbalances.

104.04 The Phenotype of 16p11.2 Microdeletion and Microduplication. E. Hanson*[1], R. Hundley[1], A. Fong[2], M. Shahab[2], J. Doerr[2], A. Lian[2], K. Greenberg[2], C. Davit[1], A.

Johnston[2], C. Tam[2], H. Peters[2], K. Lowe[2], S. J. Brewster[2], M. M. Sobeih[2], R. Nasir[2], M. Gregas[2] and D. Miller[2], (1)*Children's Hospital*, (2)*Children's Hospital Boston*

Background: Autism Spectrum Disorders (ASD) are neurodevelopmental disorders known to have a strong genetic basis. Two recent papers described microdeletions and microduplications on chromosome 16 (16p11.2) in large samples of children previously diagnosed with ASD (Weiss et al, 2008; Kumar et al, 2008). This de novo mutation seemed to account for approximately 1% of cases of ASD (Weiss et al, 2008) but the phenotypic spectrum of 16p11.2 cases has not been well described.

Objectives: Describe the cognitive and behavioral phenotype of a group of 12 children (aged 2-18 years) from a hospital population diagnosed with microdeletions and microduplications at 16p11.2.

Methods: A convenience sample of 12 families participated in the study and have completed a phenotyping battery consisting of standardized measures of cognitive ability, adaptive skills, and behavioral functioning, including the ADOS and ADI. Blood samples were drawn from each participating family member for DNA and RNA isolation as well as cell line creation. Additional measures were completed with other family members including the Family History Interview for participating parents and measures of adaptive skills and behavioral functioning for participating siblings.

Results: Four probands met criteria for ASD on both the ADOS and ADI. An additional two probands met ASD criterion on the ADOS but not the ADI, and another three probands met ASD criterion on the ADI but not the ADOS. Thus, 9 of 12 probands met criterion for ASD on at least the ADOS or ADI. Nonverbal intelligence scores (NVIQ) ranged from standard scores of <49 (<1st percentile) to 131 (98th percentile) (Mean = 81; median = 81). Verbal intelligence scores (VIQ) ranged from <49 (<1st percentile) to 111 (77th percentile). (mean = 80, median = 85).

The majority of children exhibited language delay, with eight probands acquiring single words at or after age 24 months and nine acquiring phrases at or after age 33 months. There was reduced reporting of regression and increased reporting of high activity level similar to that described by Weiss et al.(2008).

Conclusions: To the best of our knowledge, we have behaviorally phenotyped the largest group of children with the recently described 16p11.2 microdeletion/duplication. We found that children with the 16p11.2 microdeletion/duplication have an extremely varied phenotype. Seventy-five percent of our population meet criterion for ASD on either the ADOS or ADI, or both, as well as when based on clinical impression. In addition, cognitive, adaptive and behavioral profiles are extremely varied. Larger studies will be needed to fully characterize these children. We continue to recruit subjects and analyze results.

104.05 Amyloid Precursor Protein-Binding Protein (APBA2) Is An Autism Candidate Gene. T. D. Babatz*, R. A. Kumar, J. Sudi, W. B. Dobyns and S. L. Christian, *University of Chicago*

Background: Copy number variation (CNV) and resequencing analyses have implicated several autism candidate genes related to the structure and function of the synapse, including *NRXN1*, *NLGN3* and *NLGN4*, *SHANK3*, and *CNTNAP2*. We have previously reported an autistic proband and affected brother with two maternally-inherited microduplications located in 15q13.1 and 15q13.3. Duplication and deletion of an overlapping interval within 15q13.1 have been reported in patients with schizophrenia and mental retardation, respectively. The amyloid precursor protein-binding protein A2 (*APBA2*) gene is located within the 15q13.1 region and encodes a neuronal adaptor protein essential to synaptic transmission that interacts directly with NRXN1 at the presynaptic membrane. We hypothesize that APBA2 may be an additional synaptic protein associated with autism.

Objectives: To screen *APBA2* for rare nucleotide variation in autistic individuals and controls.

Methods: PCR-based Sanger sequencing of genomic DNA was used to screen *APBA2* in 372 autism samples and 372 control individuals. Autism samples were acquired from the Autism Genetics Resource Exchange (AGRE) and controls from the NIMH Genetics Initiative control sample set. Family members were acquired to determine inheritance patterns and segregation of the autism phenotype with identified variants. Bioinformatics approaches were used to predict effects of variants on protein function.

Results: We identified eight novel autism-specific non-synonymous coding variants in *APBA2*, seven of which are predicted to affect protein function by

at least one prediction program and/or alter residues that are conserved across all 28 species examined. Four variants occur in the MUNC18-interacting domain or PDZ domains of APBA2, which are essential to its neuronal function. We identified two non-synonymous variants specific to controls. These data suggest a trend of increased mutation burden in our autism cohort compared to controls (Fisher exact test p = 0.11). All autism-specific variants were inherited from unaffected parents. Of particular interest were two variants that were identified in the same proband: (1) a paternally-inherited heterozygous 6-bp deletion in exon three that causes deletion of two amino acid residues and substitution of a third, and (2) a maternally-inherited heterozygous missense mutation in exon 11. Both variants were also observed in an affected sibling. These results suggest compound heterozygous mutations of *APBA2* in both siblings with autism.

Conclusions: This work represents the first sequence-level evaluation of *APBA2* as an autism candidate. Although all eight non-synonymous variants are inherited, we hypothesize that rare variation of *APBA2* may underlie risk for autism. The co-occurrence of two non-synonymous mutations in both affected siblings in a single family, each transmitted from a different unaffected parent, may indicate a causative role for *APBA2* mutations in this isolated case. Functional studies to evaluate the effects of these mutations on the interaction of APBA2 with MUNC18-1 and NRXN1 are necessary. Taken together, the observation of rare CNVs involving *APBA2* in autism, schizophrenia, and mental retardation, the observation of a trend towards increased mutation burden in autistic individuals, and the occurrence of compound heterozygous mutations in a single family provide strong support for *APBA2* as a candidate gene for autism.

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105.01 1 An Integrative Molecular Concept Modeling of GxE Interactions in Autism. C. Hicks*, G. Steinhardt, J. Del Greco and A. Tchourbanov, *Loyola University Medical Center*

Background: Over the last decade autism has emerged as a major pandemic affecting 1 out of 160 children in the. Autism is a behaviorally defined syndrome that is diagnosed on the basis of clinical history. Currently there are no known genetic markers. Diagnostic criteria include presence before the age of three of language impairment, social reciprocity deficits and a tendency to engage in repetitive behavior. Family and twin studies have firmly established the roles of genes and environment in autism. Despite this knowledge defining the genetic architecture of autism spectrum disorder (ASD) remains a central challenge. One of the more significant bottlenecks is the inability to conduct research that incorporates gene by environment interactions in study designs and analysis strategies.

Objectives: To determine whether autism candidate genes are functionally related and interact with environmental response genes within pathways.

Methods: We performed pathway prediction and network modeling to elucidate GxE interactions at molecular level. We hypothesized that autism candidate genes and environment response genes interact within pathways, and are functionary related. We used 238 autism candidate genes identified through knowledge discovery, and 654 environment response genes from the Environmental Genome Project to test this hypothesis.

Results: We have shown that autism candidate genes and environment genes are functionally related and interact within pathways. Among the sets of genes identified include the interleukins.

Conclusions: This analysis reveals complex interactions and highlights the potential role of environment in gene regulation and function.

105.02 2 Anatomical Phenotyping in a Mouse Model of Fragile X Syndrome Using Magnetic Resonance Imaging and Computed Tomography. J. Ellegood*[1], L. K. Pacey[2], D. R. Hampson[2], J. P. Lerch[1] and R. M. Henkelman[1], (1)*The Hospital for Sick Children*, (2)*University of Toronto*

Background: Phenotyping in the mouse brain using Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) has been shown to be quite useful in determining specific changes in the brain and skull (Neiman et al., Physiol Genomics, 2006). Fragile X Syndrome (FXS) is the most common cause of mental retardation and can be linked to a specific gene. The Fragile X knockout mouse (FX KO) is the most widely used animal model of FXS (Dutch-Belgian Fragile X Consortium, Cell, 1994).

Objectives: The purpose of this study was to assess differences between FX KO and wild type (WT) mice using a variety of imaging methods.

Methods:

Fourteen male C57/B6 fixed mice brains were examined (7 WT and 7 FX KO).

MRI Acquisition - A 7.0 Tesla MRI scanner (Varian Inc.) was used to acquire anatomical images of brains within skulls as well as Diffusion Tensor Images (DTI) to assess changes in the white matter. Total imaging time was ~11 h and 16 h for the two methods, respectively.

CT Acquisition – Three dimensional CT data sets were acquired using a micro CT scanner (GE Medical Systems). The computed images show calcified bone as highly intense against a relatively uniform dark background. Imaging time was ~2.5 h.

Data Analysis - To visualize and compare changes, the images were registered. Volumes were calculated from the anatomical images by using deformation fields for each individual brain from the segmented population average. From this data the volume of 62 different structures were assessed. Changes in white matter were determined from Fractional Anisotropy (FA) maps which were created and registered from the DTI data set. FA is a scalar measure of the degree of anisotropy in the tissue and it ranges from 0 to 1, where 0 is isotropic (i.e. the tissue has no order or spherical symmetry, gray matter) and 1 is highly anisotropic (i.e. the tissue is highly ordered, white matter). Skeletal changes were also assessed using the registered CT images.

Results: Significant volume differences were found in 3 regions, a decrease in the arbor vita of the cerebellum and the striatum, and an increase in the cerebral cortex of the parieto-temporal lobe. The most significant difference was the arbor vita of the cerebellum, $p=0.0002$, false discovery rate = 1.5%. The cerebellum, therefore, was examined on a voxel by voxel basis to determine where the changes were localized. The significant decreases in the cerebellum seem to be located in specific nuclei such as the dentate nucleus and the nucleus interpositus. No significant differences in FA were found between the FX KO and WT, and in spite of the facial dimorphism that is common in human FXS we did not find any significant skeletal changes between groups.

Conclusions: This study shows specific volumetric changes within the cerebellum in Fragile X syndrome. No changes were found in both the white matter and skeletal assessment of the FX KO mouse; however, changes may be found in other Autism Spectrum Disorders.

105.03 3 $5HT_{1A}$, Benzodiazepine and NMDA Receptor Binding in Broca's Area in Autism. M. Simms*, A. Oblak, T. Gibbs and G. Blatt, *Boston University School of Medicine*

Background: Language and communication deficits are often the first presenting symptoms in individuals with autism. Language functioning in these individuals presents as a phenotypically diverse spectrum of linguistic abilities and deficits—in semantic, syntactic, pragmatic and phonologic linguistic categories. These linguistic deficits may be related to disturbed functioning and connectivity of language related brain regions. One of the primary functions of Broca's area, the opercular (BA44) and triangular (BA45) premotor regions of the inferior frontal gyrus, is speech production. Neuroimaging studies of individuals with autism engaged in language tasks report abnormal asymmetry and activation patterns in Broca's area as well as evidence of altered connectivity between Broca's area and other language related brain regions. It is likely that receptor/synaptic-level deficits in part underlie this reported malfunctioning of Broca's area in autism. Previously, our laboratory found alterations of GABA and serotonin (5HT) receptor subtypes in brain regions involved with social communication. GABA, serotonin and glutamate are suggested to be influential in the etiology, symptoms and treatment of autism. Understanding the neurochemical profile of these receptor subtypes in Broca's area in autistic individuals may help identify some of the key neural substrates underlying these abnormalities and may direct future studies aimed at treating core neural impairments related to language deficits in the disorder.

Objectives: To determine the density of 5HT1A, benzodiazepine, and NMDA receptor binding sites in superficial (I-IV) and deep layers (V-VI) of Broca's area (BA44-45) in adult autism and matched control cases.

Methods: In Broca's area, single concentration receptor binding studies were completed for 5HT1A (^{3}H-8-OH-DPAT), benzodiazepine (^{3}H-Flunitrazepam), and NMDA (^{3}H-MK-801) receptors in autism (n= 4-6) and control (n= 8-9) fresh

frozen human postmortem 20 µm thick tissue sections from the left hemisphere matched for age and post-mortem interval. Optical densities were measured in superficial and deep layers of Broca's area using the Inquiry program. Student t-tests compared superficial layers, deep layers, and superficial and deep layers combined in Broca's area by group.

Results: There was a significant overall reduction in the density of NMDA receptors (p=0.03) in the combined superficial and deep layers of Broca's area in autism. Also, there was a trend toward a reduction in the density of NMDA (p=0.09) and 5-HT1a (p=0.07) receptors in the superficial layers in the autistic group. In contrast, there were no significant findings or trends in benzodiazepine binding site densities in Broca's area.

Conclusions: The significant overall reduction in NMDA receptor density in superficial and deep layers combined and a trend toward a reduction of NMDA and 5HT1A receptors in superficial layers suggest that these specific receptor subtypes may contribute to the underlying synaptic connectivity disturbances in Broca's area in autism.

Acknowledgements: We gratefully acknowledge a grant from the Nancy Lurie Marks Family Foundation. Tissue specimens were obtained from the Harvard Brain and Tissue Resource Center, the NICHD Brain and Tissue Bank for Developmental Disorders and The Autism Research Foundation.

105.04 4 Early Increase in Serotonin Axons in Autism Brain Results in Dystrophic Fibers and Glial Reactivity. E. C. Azmitia*[1], P. Whitaker-Azmitia[2], Z. P. Hou[1] and J. Wegiel[3], (1)*New York University*, (2)*State University of New York*, (3)*New York State Institute for Basic Research in Developmental Disabilities*

Background: Studies of autistic boys aged 2-5 years using PET indicate that serotonin in the frontal cortex and thalamus is lower than in control subjects (Chugani et al., 1999). There are reports that serotonin drugs may be helpful in alleviating some of the symptoms of autism (Hollander et al, 2007). If serotonin levels are increased, anxiety and repetitive behaviors are improved (Kolevzon et al 2006); and if reduced, the symptoms worsen in children with autism (McDougle et al., 1996). There may be an association between autism and particular polymorphisms of the serotonin transporter gene (Singh et al, 2007). An increase in blood serotonin levels of children with autism has been long noted (Schain and Freedman 1961; Minderaa et al, 1989; Janusonis 2008). There are a number of theories of how damage to the serotonin system may lead to autism (Casanova, 2007) and several animal autism models are based on manipulation of the serotonin system early in development (Whitaker-Azmitia, 2001; Boylan et al, 2007). "Overall, serotonin appears to have the most empirical evidence for a role in autism." Lam et al (2006). However, to date, no direct studies of serotonin have been reported in postmortem brain. Objectives: Label serotonin axons in medial forebrain bundle and in subcortical and cortical telencephalic structures and determine if there are age-related changes in autism and typical control donors. Study any accompanying changes in astrocytes and microglial cells with dual 5-HTT labeling. Methods: The age-related (2-33yrs) profiles of serotonin axons (5-HTT antibody) and supporting astrocytes (GFAP antibody) and microglial (IBA-1 antibody) cells are immunoreactive (IR) with a transporter antibody in post-mortem tissue from autistic (2-34 years; n=7) and typical control (2-33 years; n=7) donors. All tissue was obtained from Autism Tissue Program. Diamonio-benzidine and HRP procedure, with or without Nickel enhance was used to visualize cells. Immunoreactive density and morphometric studies using NIH Image J system to estimate the number and occurrence of dystrophic fibers. Results: 5-HTT-IR axons in autism, in contrast to typical control, show region specific changes. 5-HTT-IR axons in MFB, septum and preoptic area are increased in autism compared to typical controls, while axons in temporal cortex and hippocampus are reduced at all ages studied. Dystrophic 5-HTT-IR fibers were seen in amygdala and temporal cortex in the brains from older autistic patients (12-29 yrs.). In temporal cortex of autism donor, astrocytes are reactive at all ages while microglial cells are reactive only at the youngest age. Conclusions: The current hypothesis is that in brains from autistic donors, serotonin axons in telencephalon peak early in subcortical structures but maintain depressed levels in cortical structures due to loss of astrocytic trophic functions. Dystrophic 5-HTT-IR fibers appear similar to those in neurodegenerative diseases (Azmitia and Nixon, 2008). Diet, exercise, light and drug treatments to decrease serotonin actions early in childhood but increase serotonin action in adolescence-adult periods may prove beneficial.

105.05 5 Clathrin Is Altered in the Brain of Autistic Children. A. Sheikh*[1], X. Li[1], G. Y. Wen[2], W. T. Brown[2] and M. Malik[1],

(1)*NYS Institute for Basic Research in Developmental Disabilities*, (2)*New York State Institute for Basic Research in Developmental Disabilities*

Background: Clathrin is a protein that is the major constituent of the "coat" of clathrin-coated pits and coated vesicles that are formed during endocytosis of materials at the surface of cells. Clathrin proteins have been implicated in synaptic plasticity. Clathrin assembly protein 3 (AP-3), which is a neuron-specific component of clathrin coated vesicles has been suggested to play a regulatory role in synaptic vesicle recycling since it promotes the assembly of uniform clathrin cages. Scientists have long hypothesized that impairing normal synaptic plasticity might lead to schizophrenia or autism. Very recently a study reported that microRNAs are differentially expressed in autism as compared with age-matched controls and suggested that these microRNAs are very important in regulating synaptic plasticity.
Objectives: The aim of this study is to examine whether clathrin is involved in the pathogenesis of autism by determining the expression levels of clathrin in the brain of autistic individuals and the age-matched controls
Methods: Frozen human brain tissue (frontal cerebral cortex) of autistic patients and age matched control subjects were obtained from the NICHD Brain and Tissue Bank for Developmental Disorders. Donors with autism fit the diagnostic criteria of the Diagnostic and Statistical Manual-IV, as confirmed by the Autism Diagnostic Interview-Revised. Participants were excluded from the study if they had a diagnosis of fragile X syndrome, epileptic seizures, obsessive–compulsive disorder, affective disorders, or any additional psychiatric or neurological diagnoses. This study was approved by the Institutional Review Board of the NY State Institute of Basic Research. In this study, Western Blot Analyses were used to detect the expression levels of clathrin in the brain homogenates.
Results: Our studies show that clathrin is significantly reduced in the brain of autistic children in comparison with age matched controls.

Conclusions: The result from our studies suggests that clathrin may be involved in the pathogenesis of autism by impairing normal synaptic plasticity.

105.06 6 Increased Activities of Brain Na+-K+-ATPase and Ca2+-Mg2+-ATPase in Frontal Cortex and Cerebellum from Autism. V. Chauhan*[1], L. Ji[1], B. Muthiayah[1], W. T. Brown[2] and A. Chauhan[1], (1)*NYS Institute for Basic Research in Developmental Disabilities*, (2)*New York State Institute for Basic Research in Developmental Disabilities*

Background: The enzymes Na^+-K^+-ATPase and Ca^{2+}-Mg^{2+}-ATPase are ubiquitously present and they maintain intracellular gradients of ions that are essential for signal transduction.

Objectives: To compare the activities of Na^+-K^+-ATPase and Ca^{2+}-Mg^{2+}-ATPase in brain homogenates from frontal, temporal, parietal, and occipital cortex and cerebellum from autism subjects with an age range of 4 to 39 yrs (N = 7 to 10 for different regions) and age-matched control subjects (N = 9 to 10).

Methods: Na^+-K^+-ATPase and Ca^{2+}-Mg^{2+}-ATPase hydrolyze the ATP into ADP and inorganic phosphorus. Inorganic phosphorus thus released was assayed by measuring the inorganic phosphorus.

Results: The activities of both Na^+-K^+-ATPase ($p < 0.05$) and Ca^{2+}-Mg^{2+}-ATPase ($p < 0.001$) were significantly increased in the cerebellum in the autism samples as compared to age-matched controls. The activity of Na^+-K^+-ATPase ($p < 0.05$) but not Ca^{2+}-Mg^{2+}-ATPase was increased in the frontal cortex in the autism samples as compared to age-matched controls. In contrast, the activities of these enzymes were not different between autism and control groups in other regions of brains, i.e., temporal, parietal and occipital cortex.
Conclusions: We propose that increased activities of Na^+-K^+-ATPase and Ca^{2+}-Mg^{2+}-ATPase in frontal cortex and cerebellum may contribute, in part, to altered neocortical circuit functions in autism.

105.07 7 Elevated Cytokines in the Brain of Autistic Individuals. X. Li*[1], A. Chauhan[1], A. Sheikh[1], S. Patil[2], V. Chauhan[1], X. M. Li[2], L. Ji[1], W. T. Brown[3] and M. Malik[1], (1)*NYS Institute for Basic Research in Developmental Disabilities*, (2)*Mount Sinai School of Medicine*, (3)*New York State Institute for Basic Research in Developmental Disabilities*

Background: Although the pathogenesis of autistic spectrum disorders (ASD) is not understood, recent studies have suggested that localized inflammation of the central nervous system may contribute to the pathogenesis of ASD. A number of studies have shown that TNFα, IFNγ, IL-1β and IL-12 were increased in the peripheral blood of ASD subjects. However, it is difficult to interpret these findings with respect to the pathogenesis of ASD since it is not clear that the immune findings in peripheral blood

mononuclear cells in autistic subjects correlate with immune-mediated pathology within the central nervous system. Recently, it has been reported that TNFα was increased in the cerebral spinal fluid of autistic patients. However, only one study has been conducted to investigate the inflammatory cytokine profile in the brain of autistic individuals using a cytokine protein array method (Vargas et al., 2005).

Objectives: The aim of this study is to further investigate whether immune-mediated mechanisms are involved in the pathogenesis of autism and gain a clearer picture of cytokine activities in the brain of autistic individuals.

Methods: Invitrogen's Multiplex Bead Immunoassays (Human Cytokine 10-plex) were used to determine the levels of different cytokines in the cerebral front cortex from 8 autistic subjects and age-matched controls. Cytokine levels were measured with a Luminex 200™ system (Bio-Rad Laboratories). Raw data (mean fluorescent intensities) were analyzed by Bio-Plex Manager Software 4.1 version (Bio-Rad Laboratories) to obtain concentration values.

Results: Our results showed that proinflammatory cytokines (TNF-α, IL-6 and GM-CSF), Th1 cytokine (IFN-γ) and chemokine (IL-8) were significantly increased in the brains of ASD subjects compared with the controls. However the Th2 cytokines (IL-4, IL-5 and IL-10) showed no significant difference. The Th1/Th2 ratio was also significantly increased in ASD patients.

Conclusions: ASD patients displayed an increased innate and adaptive immune response through the Th1 pathway, suggesting that localized brain inflammation and autoimmune disorder may be involved in the pathogenesis of ASD.

105.08 8 Delayed Development of Neurons in Networks Involved with Stereotypic Behaviors and Reward in Autism. K. Nowicki*[1], I. Kuchna[1], S. Y. Ma[1], J. Wegiel[1], T. Wisniewski[1], I. L. Cohen[2], E. London[1], M. J. Flory[1], W. T. Brown[1] and J. Wegiel[1], (1)*New York State Institute for Basic Research in Developmental Disabilities*, (2)*NYS Institute for Basic Research in Developmental Disabilities*

Background:

Autism signs include lower-order repetitive motor behaviors, intense circumscribed patterns of interests, and higher-order rituals and compulsions that occur regularly and interfere with daily functioning (Gabriels et al., 2005). Several studies have implicated the role of basal ganglia and frontostriatal circuitry in the pathophysiology of autism, especially in repetitive and stereotyped behaviors. Increased volume of the basal ganglia was reported in several MRI studies (Herbert et al., 2003; Hollander et al., 2005; Langen et al., 2007; Sears et al., 1999). However, the nature of cellular changes in the basal ganglia is unknown.

Objectives:

We suggest that the application of sensitive, unbiased morphometric methods may reveal cellular developmental changes in the striatum that contribute to the restricted repetitive and stereotyped behavior in autistic subjects. The presence of changes in the nucleus accumbens could be an indicator of the abnormal function of the reward system. We hypothesize also that changes in the reward system may amplify repetitive and stereotyped behaviors in early childhood.

Methods:

To test this hypothesis, we examined the caudate nucleus, putamen and globus pallidus, contributing to restricted repetitive and stereotyped behaviors, and the nucleus accumbens, which is a component of the reward system, in the brains of 14 subjects diagnosed with idiopathic autism and of 14 age-matched controls. The Cavalieri method was applied to evaluate the volume of the examined structures; the fractionator method, to estimate the number of neurons; and a nucleator, to estimate the volume of neurons and nuclei.

Results:

Our study showed a significantly smaller size of neurons in the caudate, putamen, and globus pallidus in the brains of autistic children 4 - 8 years of age. This suggests a developmental delay in the growth of neurons, which may contribute to the dysfunction of all components of the basal ganglia network. The significant developmental delay of neuron growth in the nucleus accumbens suggests that the reward system is also affected.

Conclusions:

Our results provide new evidence that developmental abnormalities in the striatal circuitry contribute to repetitive and stereotyped behaviors and that developmental changes in the nucleus accumbens may enhance engagement in rituals and stereotyped behavior.

105.09 9 Contribution of Thalamic Developmental Changes to the Autistic Phenotype. S. Y. Ma*[1], I. Kuchna[1], K. Nowicki[1], J. Wegiel[1], T. Wisniewski[1], I. L. Cohen[2], E. London[1], M. J. Flory[1], W. T. Brown[1] and J. Wegiel[1], (1)*New York State Institute for Basic Research in Developmental Disabilities*, (2)*NYS Institute for Basic Research in Developmental Disabilities*

Background: Some clinical signs of autism, such as verbal and nonverbal communication deficits, sensory abnormalities, skeletal muscle hypotonia, and cognition could be a result of developmental abnormalities in the thalamus. The lateral thalamus is closely related to language function including mechanical processes for articulation and respiration (Ojemann, 1971, 1977; Oke et al., 1978). The thalamus is involved in sensory (pain) and motor function and cognition, including memory. Pallidal input to the thalamus serves to control muscle tone. These data indicate that the thalamus may contribute to the clinical signs of autism.

Objectives: We assume that the thalamus, interacting with the neocortex and entorhinal cortex, and very closely with the amygdala and the striatal system, may have its own developmental changes contributing to motor, sensory and language deficits observed in autism. The goal of this study is to determine whether the thalamus is affected by a similar neuronal developmental delay as are the basal ganglia and cortex.

Methods: In the human thalamus, more than 50 subnuclei with specific connectivities have been identified. To detect a global pattern of neuronal development and maturation in the thalamus, rather than thalamic subregion - specific characteristics, the mean volume of neurons and neuronal nuclei was determined in the entire thalamus in 7 autistic and 7 control subjects 4 to 23 years of age. Unbiased morphometric methods of estimation of thalamic volume, number of neurons, and volume of neurons and neuronal nuclei were applied.

Results: The volume of the thalamus in autistic and control subjects is the same. However, the mean volume of neuronal soma in 4- to 8- year old children was 27% less in autistic subjects than in controls, but the difference was undetectable in older children and young adults (11-23 years old). The volume of neuronal nuclei in the youngest autistic children was reduced by 37%, whereas in older subjects, it was insignificantly higher than in controls.

Conclusions: A smaller volume of the cell body and cell nucleus in thalamic neurons in the youngest autistic children and an almost normal size in late childhood and adulthood suggests a significant delay of neuronal growth in the early stages of brain development and acceleration of growth in late childhood compensating for developmental deficits. The presence of a similar developmental delay of neuronal growth in the thalamus and the neuronal networks interacting with the thalamus suggests that each component of these complex neuronal networks may make its own contribution to the clinical phenotype of autism.

105.10 10 Developmental Heterochronicity of Neuron Growth in the Memory System of Autistic Subjects. I. Kuchna*[1], K. Nowicki[1], J. Wegiel[1], S. Y. Ma[1], T. Wisniewski[1], I. L. Cohen[2], E. London[1], M. J. Flory[1], W. T. Brown[1] and J. Wegiel[1], (1)*New York State Institute for Basic Research in Developmental Disabilities*, (2)*NYS Institute for Basic Research in Developmental Disabilities*

Background: Reduced volume of both the hippocampal formation and the amygdala were noted in subjects examined by Aylward et al. (1999), but not in populations examined by other researchers (Piven et al., 1998). Smaller and more densely packed neurons were found in various portions of the hippocampal formation, entorhinal cortex and medial nuclei of the amygdala (Bauman and Kemper, 1985; Kemper and Bauman, 1993).

Objectives: We hypothesize that postmortem morphometric studies will help to identify the type, distribution and severity of developmental abnormalities in major components of the memory system. These may contribute to memory system abnormalities in a structure-specific way. The entorhinal cortex is a developmental hybrid providing major input from association cortices and the amygdala to the hippocampus. The hippocampus is involved in processing and storage of information. The amygdala is the component of the memory system that processes social and emotional signals.

Methods: To test this hypothesis, we examined neurons in entorhinal cortex layers II, III, V and VI; in cornu Ammonis sectors 1, 2, 3 and 4; and in four nuclei of the amygdala of 10 autistic and 10 control subjects 4 to 56 years of age. Unbiased morphometric methods of estimation of brain structure volume, number of neurons and volume of neurons and neuronal nuclei were applied.

Results: Finding a reduced size of neurons in 4 to 8 years old children in layer II (islands) by 20%, in layer III by 33%, and layers V and VI by 33% and 26%, respectively, and a similar range of reduction of size of neurons in the amygdala (from 22% in accessory basal to 34% in basal nucleus), but the lack of a significant difference in the volume of neurons in all four sectors of the cornu Ammonis suggests that the memory system is affected in an early stage of brain development but in a structure-specific way.

Conclusions: The cornu Ammonis does not show a pattern of cortical and basal ganglia developmental delay. Selective preservation of the developmental pattern of neurons in the cornu Ammonis involved in storage of information from affected structures including the entorhinal cortex and amygdala may help explain memory abnormalities mixed with restricted interests and abilities.

105.11 11 Mapping of Oxidative Stress Damage in Autistic Brain. E. M. Sajdel-Sulkowska*[1], M. Xu[2], W. McGinnis[3] and N. Koibuchi[2], (1)*Harvard Medical School/BWH*, (2)*Gunma University Graduate School of Medicine*, (3)*Autism House, Autism New Zealand*

Background: Increased oxidative stress and associated protein modification measured by 3 nitrotyrosine (3-NT) has been reported in over fifty different pathologies. We have previously shown increased 3-NT levels in autistic cerebella.

Objectives: The aim of the current study was to identify brain regions in autism with the highest level of oxidative damage by mapping the levels of 3-NT across brain regions.

Methods: The levels of 3-NT were measured by ELISA in brain homogenates prepared from frozen brain samples. The levels of 3-NT were analyzed in 13 individual brain regions of an autistic male donor (age 14.3 years; PMI 9 hours) and matched control male donor (age, 14.5 years; PMI, 16 hours).

Results: In contrast to control brain where the levels of 3-NT were uniformly across regions examined, ranging from 2.86 pmol/g to 10.54 pmol/g, in autistic brain the 3-NT levels were variable ranging 1.68pmol/g to 151.39pmol/g. Several autistic brain regions showed increased 3NT levels; the highest 3-NT levels were observed in Wernicke's area > cerebellar hemisphere > orbitofrontal gyrus > cerebellar vermis > hippocampus. The increase, expressed as percent control, ranged from 4955 in Wernicke's area to 286 in hippocampus. There was no increase in 3-NT levels in prefrontal cortex, caudate, cingulate gyrus, corpus callosum, corona radiate, putamen and thalamus in autistic brain.
Conclusions: The increase in oxidative stress damage in autism appears to be brain region-specific and most pronounced in brain areas associated with the speech processing, sensory and motor coordination, emotional and social behavior and memory, a pattern consistent with clinical manifestations of autism. At this point it is not clear whether this pattern of oxidative stress is common to a subclass of autism spectrum. These data, however, suggest that we may begin to relate oxidative changes to autistic pathology and perhaps also identify new brain regions involved in autism by mapping oxidative stress damage across brain regions.

105.12 12 Minicolumnar Core Width by Lamina in Brains of Patients with Autism. M. F. Casanova, P. Narahari*, A. S. El-Baz, E. A. Vanbogaert and A. E. Switala, *University of Louisville*

Background: Minicolumns are modular elements of organization found within the neocortex of all examined mammalian species. Within a minicolumn there may be distinguished a core, comprising the cell somata, axons, and apical dendrites of pyramidal cells, and a periphery, comprising other processes and few cell somata, mostly interneurons. Postmortem studies examining the radial organization of pyramidal cell arrays in people with autism suggest the presence of smaller minicolumns, compared to normal controls.

Objectives: This study further characterizes this cortical deficit by comparing core width (*w*) minicolumnar width across laminae. It was our initial hypothesis that minicolumnar width differences in autism would be most prominent in supragranular laminae.

Methods: Brains from six autistic patients (diagnosed according to DSM IV-TR and ADI-R)

and an equal number of age-matched controls were celloidin embedded, sectioned at 200 μm or 500 μm, and Nissl stained with gallocyanin. Photomicrographs mosaics of the cortex from nine different brain regions (cortical areas 3b, 4, 9, 10, 11, 17, 24, 43, and 44) were subjected to computerized image analysis for minicolumnar core width. Statistical analysis employed a linear mixed effects model, with case-control pair as a random effect and fixed effects diagnosis (autistic disorder or none), cortical area, and lamina (II+III, IV, or V+VI) together with all interaction effects, and also sex and cerebral hemisphere.

Results: Statistically significant differences were found by diagnosis ($F_{1,263} = 554.0$; $P < 0.0001$), cortical area ($F_{8,263} = 2.69$; $P = 0.0073$), lamina ($F_{2,263} = 630.0$; $P < 0.0001$), diagnosis×cortical area interaction ($F_{8,263} = 4.95$; $P < 0.0001$), and diagnosis×lamina interaction ($F_{2,263} = 45.06$; $P < 0.0001$). The interaction of all three effects was not statistically significant ($F_{16,263} = 1.55$; $P = 0.0836$). Autistic subjects had core widths measuring 69 %, 74 %, and 65 % of those in matched controls in supragranular laminae, lamina IV, and infragranular laminae, respectively. The greatest differences between autistic patients and controls were found in area 44, where $w = 4.84$ μm and $w = 8.98$ μm, respectively. Within any given region and diagnostic category, it held without exception that core width increased with depth: $w_{V+VI} > w_{IV} > w_{II+III}$.

Conclusions: Previous studies suggest that minicolumnar narrowing in autism is accounted for the greater part by reduction of peripheral neuropil space. We have now shown some diminution in the minicolumnar core. Our initial hypothesis was not borne out, and the fact that minicolumns appear to be diminished in width across laminae suggests involvement of a shared constituent among the different layers, e.g., double bouquet and pyramidal cells. Opercular area 44 is part of Broca's area in humans. The role of this area in language processing, speech production, and understanding the intention behind observed motor acts makes the reported finding a potential clinicopathological correlate to autism.

105.13 13 Reduced Gyral Window and Corpus Callosum Size in Autism: Possible Macroscopic Correlates of a Minicolumnopathy. M. F. Casanova*[1], A. S. El-Baz[1], M. C. Mott[1], G. B. Mannheim[2], H. Hassan[1], R. Fahmi[1], J. N. Giedd[3], J. M. Rumsey[3], A. E. Switala[1] and A. A. Farag[1], (1)*University of Louisville*, (2)*Food and Drug Administration*, (3)*National Institute of Mental Health, National Institutes of Health*

Background: Minicolumnar changes that generalize throughout a significant portion of the cortex have macroscopic structural correlates that may be visualized with modern structural neuroimaging techniques. Minicolumns in the brains of autistic patients were narrower and more numerous per linear length of tissue section examined as compared to controls. Since the minicolumn re-iterates itself millions of times throughout the brain, variations in the total number and width of minicolumns can result in macroscopic changes of the brain's surface area and/or gyrification. Furthermore, proper integration of supernumerary minicolumns, both into corresponding segregates and their lateralized hemispheric homologues, requires their interconnectivity via association and commissural fibers.

Objectives: In this study, a series of autistic patients were studied for gross morphometric parameters related to minicolumnar pathology: cortical thickness (*t*), gray/white matter ratio (*G:W*), corpus callosum shape (*CC*) and cross-section (*CCx*), cortical folding, adjusted for age (GI_{adj}), and median white matter depth (*w*), as a proxy measurement for gyral window.

Methods: Fourteen male subjects between 8 and 38 years of age were recruited from across the. DSM-III-R and the Autism Diagnostic Interview (ADI) criteria were used to define autism, autistic disorders, and pervasive developmental delay. Twenty eight male, non-autistic individuals, matched 2:1 with patients for age and handedness, were recruited for comparison. Subjects were scanned on a 1.5 T GE MRI using IR and FLASH volume sequences. Images were preprocessed to reduce scanner noise. A deformable model was fit to the white matter surface of each brain, and morphometric parameters were computed from this model (*w*, *CC*) or directly from the MRI slices (GI_{adj}, *t*, *CCx*, *G:W*).

Results: There was a significant difference between the gyral window of autistic and normal control subjects. The cumulative distribution functions (CDF) of individual patients cluster tightly around the average CDF for their

respective diagnostic categories. The gyral window *w* averaged 2.4 mm in autism and 5.8 mm in controls, and *w* was highly correlated with *CC* within diagnostic categories (R^2 = 0.9966). *CCx* was reduced in patients with autism (5.3 cm^2) relative to controls (6.6 cm^2). There was no significant diagnosis dependence in *t* or GI_{adj}, and the latter did not correlate significantly with *w*.

Conclusions: A reduced gyral window constrains the possible size of projection fibers and biases connectivity towards shorter corticocortical fibers at the expense of longer association/commisural fibers. The normal maturation processes of enlarging cell somata, myelination, synaptogenesis, and increased dendritic branching manifest themselves as exuberant brain growth early in life only to be followed by the loss of those less efficient connections (long association fibers) that are constrained by the reduced aperture of the gyral window. These retractive events fall within a spectrum spanning normal individuals and autistic patients. The findings may help explain abnormalities in motor skill development, differences in postnatal brain growth, and the regression of acquired functions observed in some autistic patients.

105.14 14 Exploring the Association Between Amygdala Volume and Cortisol Responsivity in Children with Autism. B. Corbett*[1], C. Schupp[1], N. Ryan[1] and V. Carmean[2], (1)*M.I.N.D. Institute, University of California at Davis*, (2)*University of Colorado, Denver*

Background: Children with autism often exhibit impairment in socioemotional processing and enhanced stress in novel situations. The amygdala, which is involved in these processes, has long been implicated in the neuropathology of autism. Previously we have reported significant variability in diurnal regulation and stress responsivity of cortisol in children with autism. Similarly, we have shown notable variability in the volume of the amygdalae in autism, and subsequent within-group analysis revealed that smaller right amygdala volume was associated with more social anxiety.

Objectives: The current investigation was designed to compare neuroimaging and psychobiological data across study participants to determine if an association exists between cortisol stress responsivity and amygdala volume.

Methods: The study included 26 children ages 8-to-12 years old with autism (*n*=12) and typical development (*n*=14) that participated in the cortisol regulation and responsivity and neuroimaging protocols. Using correlation analysis and linear regression we: 1) compared the relationship between amygdala volume and cortisol across participants, 2) assessed associations between stress, amygdala volume and diagnosis, and 3) evaluated the relationship between stress responder status and amygdala volume in autism.

Results: There was no relationship between amygdala volume and cortisol across all of the participants or based exclusively on diagnosis. However, within the autism group, a subset emerged in children with autism that were classified as cortisol stress Responders, a classification based on elevated cortisol responsive to a stressor. The autism Responders had smaller right amygdala (t(9) = -2.73, p=0.02) and smaller left amygdala (t(9) = -3.08, p=0.01). There were no associations for autism Nonresponders or the typical Responder and Nonresponder groups.

Conclusions: The preliminary findings provide evidence for an association between enhanced LHPA responsivity and smaller amygdala in a subset of children with autism. Interestingly, smaller amygdalae have been associated with pediatric anxiety. The current findings, albeit preliminary, support our emerging hypothesis of a neuroendocrine spectrum model of autism in which individuals may ultimately be phenotyped by their stress reactivity, social anxiety and brain structure and function, which may facilitate the development of targeted treatments.

105.15 15 A Proton MRS Study of the Basal Ganglia and Dorsolateral Prefrontal Cortex in Adults with Autistic Spectrum Disorders. T. J. Lavender*[1], S. Maltezos[2], P. Johnston[3], F. Macdiarmid[1], R. O'Gorman[1], C. Murphy[3], C. Ecker[3], S. Reed[4], D. Spain[3], E. Daly[5], D. Murphy[3] and .. MRC UK AIMS Network[3], (1)*Institute of Psychiatry*, (2)*Adult ADHD Service, The Maudsley Hospital*, (3)*King's College London, Institute of Psychiatry*, (4)*South London & Maudsley NHS Trust*, (5)*Institute of Psychiatry, King's College London*

Background: There is emerging evidence that individuals with Autistic Spectrum disorders have abnormalities in neuronal integrity (and perhaps also in glutamate/glutamine(Glx)) as measured using 1H MRS. However findings have varied – possibly because some included people with co-morbid medical problems and/or mental

retardation. Also, some included children, whereas other studied adults. For example we reported that young adults with ASD have a significant increase in amygdala hippocampal Glx, and medial frontal N-Acetyl Aspartate (NAA), Choline (Cho), and Creatine and phosphocreatine (Cre) (Murphy et al 2002, Page et al 2006). In contrast others reported a reduction in NAA and Glx in other regions (for example DeVito et al 2007). NAA is correlated with mitochondrial function and neuronal integrity, Cho is a measure of membrane synthesis and turnover, and Cre is a measure of cellular energy metabolism. Prior structural and functional imaging studies have reported abnormalities in the basal ganglia and dorso-lateral pre-frontal regions in people with Autistic Spectrum Disorders. However nobody has specifically investigated the neuronal integrity of those regions using single voxel 1H MRS. Objectives: Hence we compared the neuronal integrity and concentration of glutamate/glutamine (using 1H MRS) in the basal ganglia and the dorsolateral pre-frontal cortex (together with a control (parietal) region), in non-learning disabled adults with autistic spectrum disorder and controls. Methods: We included 30 individuals with an ADI confirmed ASD (8 Asperger syndrome, 9 with Autism, and 11 with Atypical autism) and compared them to 20 age, gender and IQ matched controls. MR spectroscopy studies were performed with a 1.5T GE HDx MRI scanner (GE Medical Systems, Milwaukee, WI, USA) equipped with TwinSpeed gradients. Single voxel 1H MR spectra were acquired with a PRESS sequence with repetition time (TR) = 3000 ms and echo time (TE) = 30 ms. Voxels of interest (VOI) were positioned in the left medial parietal lobe (20x20x20 mm3) and left dorso-lateral prefrontal cortex (16x24x20 mm3), using previously described methods (Murphy et al 2002). A VOI was also positioned in the left basal ganglia (20x20x15 mm3), to include the head of the caudate, putamen, and internal capsule. MRS concentrations were corrected for VOI CSF and grey/white matter content. Results: Individuals with ASD had a significant reduction; 1) in basal ganglia concentration of Cre, NAA, and Glx, and; 2) in dorsolateral pre-frontal cortex Cre and NAA. No differences from controls were found in the parietal region. Conclusions: Adults with ASD have regionally specific abnormalities in neuronal integrity of brain regions previously implicated in the disorder, and perhaps also in the glutamate/GABA system. However, taken in combination with our prior work and that of others (Murphy et al 2002, Page et al 2006, DeVito et al 2007), our findings suggest that people with ASD do not simply have an increase, or decrease, in measures of neuronal integrity and Glx. Rather, they have a complicated mixture of both – depending upon the brain region investigated and the age of the person included.

105.16 16 Exploring the Association Between Total Cerebral Volume and Cortisol Responsivity in Children with Autism. N. Ryan*[1], C. Schupp[1], V. Carmean[2] and B. Corbett[1], (1)*M.I.N.D. Institute, University of California at Davis*, (2)*University of Colorado, Denver*

Background: Children with autism often exhibit enhanced stress in novel situations. The idea of an association between symptoms of anxiety and total cerebral volume has been proposed. Previously, we have reported significant variability in the stress responsivity of cortisol in children with autism. Similarly, we saw notable variability and a lack of gross difference in total cerebral volume between individuals with autism and control subjects. However, differences have been shown with some reports indicating cerebral enlargement. Distinctions based on age have been highlighted, hypothesizing an early, rapid brain overgrowth followed by a prolonged slowing of brain growth.

Objectives: This study was designed to compare neuroimaging and psychobiological data across study participants to determine if an association exists between cortisol stress responsitivity and total cerebral volume.

Methods: This study compared structural MRI data of overall cerebral volume with cortisol reactivity in 26 children with high functioning autism (n=12) and typical development (n=14). Using correlation analysis and linear regression we: 1) compared the relationship between total cerebral volume and cortisol across participants, 2) assessed associations between stress, total cerebral volume and diagnosis, and 3) evaluated the relationship between stress responder status and total cerebral volume in autism.

Results: There was no association between total cerebral volume and cortisol across participants or between diagnostic groups. However, within the autism group, a subset emerged showing that children classified as cortisol stress Responders, based on responsivity of the limbic-hypothalamic-pituitary-adrenal (LHPA) system to a stressor, had

larger total cerebral volume (t(8) = 2.24, p=0.04).

Conclusions: The association between stress responsivity and brain structure identifies a possible subset of autistic children while explaining some of the variance in MRI findings across studies.

105.17 17 Microstructural Connectivity of the Arcuate Fasciculus in Autism. P. T. Fletcher*[1], R. Whitaker[1], R. Tao[1], M. DuBray[1], A. L. Alexander[2], E. Bigler[3], N. Lange[4] and J. E. Lainhart[1], (1)*University of Utah*, (2)*University of Wisconsin*, (3)*Brigham Young University*, (4)*Harvard University*

Background: Language impairment in autism spectrum disorder is universal and often severe. Imaging and postmortem studies have shown abnormalities in the gray matter structures involved in language. The white matter structure of the language networks in the autism brain is unknown.

Objectives: The goal of this study was to investigate the white matter microstructure of the arcuate fasciculus in the autism brain using diffusion tensor imaging (DTI).

Methods: The data were collected as part of an ongoing longitudinal MRI study on brain development in autism. High resolution DTI was acquired from a 3T MRI scanner and analyzed on 10 individuals with autism and 10 control subjects. The arcuate fasciculus was extracted from the images using a new automated volumetric DTI segmentation algorithm. Derived measures of microstructure (fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD)) were computed in the arcuate fasciculus and compared across groups. Lateralization scores between the left and right arcuate fasciculi were computed for each diffusion measurement.

Results: As a group, those with autism displayed a significant increase in MD ($p = 0.0002$), which was due to increases in both AD ($p = 0.015$) and RD ($p = 0.009$). While there was no significant difference in the mean FA between the groups, the variance of FA was significantly greater ($p = 0.016$) in the autism group. A comparison of lateralization showed a lateralization in controls (increased FA and decreased MD on the left side) that was absent in the autism group.

Conclusions: Our findings suggest abnormal white matter microstructure in the arcuate fasciculus in autism. Furthermore, these results indicate that lateralized language specialization of the arcuate fasciculus is impaired in autism.

105.18 18 Relationship Between Corpus Callosum Structure and Intelligence in Autism and Typical Development. M. DuBray*[1], T. L. Merkley[2], E. Bigler[2], A. L. Alexander[3], A. Froehlich[1], J. E. Lee[3], J. E. Lainhart[1] and N. Lange[4], (1)*University of Utah*, (2)*Brigham Young University*, (3)*University of Wisconsin*, (4)*Harvard University*

Background: IQ is often decreased or uneven in autism, and may be related to corpus callosum (CC) development. A number of studies suggest that the corpus callosum is smaller in autism than in typical controls relative to total brain volume. We previously found smaller CC volumes and abnormal microstructure in individuals with autism. Aberrant growth of the CC could contribute to reduced interhemispheric connectivity and variations in intelligence.
Objectives: The present study examines the relationship between corpus callosum morphology and measures of intelligence and processing speed in high functioning individuals with autism.
Methods: 3T MRI T1-weighted images were used to calculate midsagittal area of the corpus callosum according to the Witelson methodology. 47 right handed males with autism (pIQ>74) were compared to 37 typically developing males (mean age: autism=12 years, controls=13.5 years).

Results: While controlling for age and total intracranial volume, significantly positive correlations were found between measures of intelligence and total callosal and subregional areas in the autism group only. In contrast, correlations were negative in controls; higher performance IQ and processing speed were related to smaller posterior callosal areas.

Conclusions: The relationship between midsagittal callosal area and intelligence differs in autism and typical development. In autism, "more is better": larger midsagittal area is related to higher IQ in autism. The opposite is found in controls in posterior CC regions. The findings suggest a fundamental difference in the relationship between the development of the corpus callosum and development of IQ in autism. Our longitudinal work, examining the trajectories of CC growth, white matter microstructural development, and the development of processing speed and intellectual skills, seeks to pinpoint

what is going on in the CC and how it affects functioning in autism.

105.19 19 Neuroanatomic Correlates of Dyspraxia in Children with Autism Spectrum Disorders. E. L. Wodka*[1], M. E. Richardson[1] and S. H. Mostofsky[2], (1)*Kennedy Krieger Institute*, (2)*Kennedy Krieger Institute, Johns Hopkins University School of Medicine*

Background: Impairments in performance of skilled motor gestures suggestive of developmental dyspraxia, are among the most consistently observed abnormalities on motor examination of children with autism. In the adult literature, apraxias are well-described, and are generally associated with impairments in left-hemisphere premotor and parietal association areas or the arcuate fasiculus connecting these regions. However, the neural underpinnings of observed praxis impairments in the developmental context of autism are not well understood.

Objectives: To examine volumetric neuroanatomic correlates of limb praxis in children with autism and typically developing (TD) children.

Methods: Thirty-five TD children (6 girls; M_{age}=10.6 +/-1.2) and 21 children with high-functioning autism (3 girls; M_{age}=10.7 +/-1.8) completed a standardized praxis examination modified for children (i.e., to include gestures learned in early and later childhood: waving good-bye, using scissors). High-resolution MPRAGE images were acquired for each subject, and analyzed using automated surface-based methods within the program, *Freesurfer*. Cortical volume measurements of regions of interest (ROI) in premotor and parietal regions were chosen based on their described relation to praxis.

Results: Groups were similar on demographic factors, with the exception of VIQ (children with autism M_{VIQ}=110.3 +/-20.4; TD M_{VIQ}=121.8 +/-12.0; $t_{(1, 52)}$=2.6,p=.012). Therefore, VIQ was used as a covariate in regression analyses examining interaction effects.

Children with autism ($M_{Total\ Errors}$=0.83 +/-0.09) performed more poorly than TD children ($M_{Total\ Errors}$=0.69 +/-0.14) on praxis exam ($t_{(1, 52)}$=4.4,p<.0001). Following Bonferroni correction (p<.01), significant negative correlations were observed in the autism group between praxis performance and left-hemisphere white matter volume in the supramarginal area (r=--0.674, p=.002); a positive correlation was observed with the left-hemisphere gray matter volume in the caudal anterior cingulate (r=0.625, p=.004). There were no significant correlations in the TD group. Additionally, there was a significant interaction between diagnosis and praxis performance with the left hemisphere white supramarginal (p=.001) and left hemisphere gray caudal anterior cingulate (p<.0001) areas, with both interactions being driven by the highly significant correlation observed in the group of children with autism.

Conclusions: The significant correlation observed between praxis performance and the supramarginal and anterior cingluate regions in the autism group is consistent with the classical schema of apraxia. A positive association with gray matter volume was observed (i.e., more gray matter associated with improved performance), suggesting that dyspraxia in autism is associated with decreased gray matter volume in the caudal anterior cingulate, important for guiding motor responses. The opposite association was observed with white matter volume in the supramarginal region, important for acquisition and storage of the perceptual representations of movement (i.e., increased supramarginal white matter volume correlated with poorer performance). Prior studies have revealed that children with autism show overgrowth of localized white matter connections and that for children with autism, increased primary motor white matter volume predicts basic motor skill impairment. Similarly, the present findings suggest that dyspraxia in autism may be associated with overgrowth of localized white matter connections in the supramarginal region, possibly reflecting fewer long-range white matter fibers connecting this region with premotor association areas.

105.20 20 A Meta-Analysis of the Corpus Callosum in Autism. T. W. Frazier*[1] and A. Y. Hardan[2], (1)*Cleveland Clinic*, (2)*Stanford University School of Medicine/Lucile Packard Children's Hospital*

Background: Several previous MRI studies have reported reductions in corpus callosum (CC) total area and several of its sub-regions in individuals with autism , supporting the aberrant connectivity hypothesis. However, studies have differed concerning the presence (3 of 10 studies report null findings), magnitude, and/or sub-region contributing to CC reductions.

Objectives: The primary aim of the present study was to meta-analytically determine the

significance and magnitude of reduction in CC total, regional, and Witelson subdivision area measures in patients with autism. The secondary aim was to examine possible moderators of total CC effects.

Methods: PubMed/Medline and PsycInfo databases were searched to identify MRI studies examining corpus callosum area in autism. Ten studies contributed data from 253 patients with autism (Mean age=14.58, SD=6.00) and 250 healthy controls (M age=14.47, sd=5.31). Of these ten studies, eight reported area measurements for corpus callosum sub-regions (anterior, mid/body, and posterior) with six studies reporting area for Witelson subdivisions. Fixed and random effects meta-analytic procedures were used to quantify autism versus healthy control differences in total and sub-region CC area measurements. Demographics and study characteristics were also coded and examined as moderators of total CC area reductions. Funnel plots and fail-safe N were used to examine possible study sampling bias.

Results: Total CC area was reduced in autism and the magnitude of the reduction was medium (Weighted Mean *d*=.48, 95% CI=.30-.66). All sub-regions showed reductions in size with the magnitude of the effect decreasing caudally (anterior d=.49, mid/body d=.43, posterior d=.37). Witelson sub-division 3 (rostral body) showed the largest effect, indicating greatest reduction in the region containing pre-/supplementary motor neurons. Funnel plots and fail-safe N indicated minimal, if any, bias in study sampling. Older participants and greater magnet strength produced larger discrepancies in total CC area between individuals with autism and healthy controls.

Conclusions: CC reductions are present in autism and support the aberrant connectivity hypothesis. Future diffusion tensor imaging studies examining specific fiber tracts connecting the hemispheres via the corpus callosum are needed to identify the cortical regions most affected by CC area reductions. Future research should also model the variance in CC area/volume to identify possible autism sub-groups.

105.21 21 MRI Morphometry of Basal Ganglia in Children with Pervasive Developmental Disorders. L. D'Errico[1], G. S. Colafati[2], F. Vatta[3], S. Calderoni[4], F. Meneghini[3], M. Marletta[1], S. Mininel[3], D. Caramella[1], C. Bartolozzi[1], S. Malena[5], A. Aragri[6], R. Tancredi[4], F. Muratori*[4] and F. Di Salle[7],

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Background: In the last decade, neuroimaging studies suggested that basal ganglia (BG: caudate nucleus, putamen and globus pallidus) are involved in the third diagnostic domain of pervasive developmental disorders (PDDs), *i.e.* repetitive interests, behaviours and activities (RIBAs). In particular, few reports (Sears *et al.*, 1999; McAlonan *et al.*, 2002; Hollander *et al.*, 2005; Rojas *et al.*, 2006) explored specifically the relationship between caudate volumes and RIBAs in PDDs. To our knowledge, however, no studies of this kind were reported on samples exclusively composed of children. On the other hand, caudate nucleus is also a structure of fronto-striatal circuit that supports executive cognitive functions, often impaired in PDDs and a recent study (Voelbel *et al.*, 2006) founded an inverse correlation between caudate volume and neuropsychological test performance in PDDs children. Furthermore, an inverse correlation between IQ and RIBAs (Cuccaro *et al.*, 2003; Szatmari *et al.*, 2006), and in particular with the lower order subgroup "sensory and motor repetitive behaviours" (Carcani-Rathwell *et al.*, 2006), has been recently reported.

Objectives: This project attempts to further assess BG morphometry in PDDs children versus matched controls. Work is in progress in order to evaluate the effects of RIBAs (assessed through the ADI-R Repetitive and Stereotyped Behavior Domain) and IQ on BG volumes.

Methods: Twenty-seven patients (19 male, 8 female) meeting DSM-IV criteria for PDDs (mean age: 66 months +/- 22) and eighteen demographically matched controls underwent a 1,5 T MRI T1 weighted acquisition. The children with PDD were evaluated with ADOS–G and with ADI-R. Patients resulted with or without associated mental retardation at non verbal IQ evaluated through WISC-R or Leiter-R (if the subject was nonverbal), while controls are composed of typically developing children. The PDDs partecipants had normal results on

screening tests for inborn errors of metabolism, normal chromosomal constitution and negative test for fragile X syndrome. Exclusion criteria included severe sensory problems, significant motor impairments or progressive neurological disorders. All the subjects were medication-naive. The anatomical T1-weighted volume is automatically segmented and meshed using Freesurfer software and BG volumes were compared between the two groups. BG have been separated into caudate, putamen and pallidus based on the regional anatomy and the volumetry of the separate structures has been analytically determined.

Results: Preliminary data indicate that differences between groups on caudate volume are not statistically significative. Nevertheless, in a subgroup of PDDs patients is possible to detect a caudate volume significantly larger then in controls. Further analysis is needed in order to correlate clinical variables with anatomical volumes.

Conclusions: These preliminary results do not give any evidence of statistically significative differences in caudate nucleus volume between PDDs children and controls. However, the hypotesis of a significant statistical correlation between BG volume with age, IQ and RIBAs scores in PDDs children calls for further investigations.

105.22 22 Total Brain Volume and Corpus Callosum Size in Medication Naïve Adolescents and Young Adults with Autism Spectrum Disorder. C. M. Freitag*[1], E. Luders[2], H. Hulst[3], K. L. Narr[2], P. M. Thompson[2], A. W. Toga[2], C. Krick[4] and C. Konrad[3], (1)*Johann Wolfgang Goethe-University*, (2)*UCLA School of Medicine*, (3)*University of Münster*, (4)*Saarland University Hospital*

Background: Increased total brain volume (TBV) has been reported for children with autism spectrum disorder (ASD), but studies in older ASD subjects have been contradictory. Similarly, studies of CC area in ASD differ with regard to inclusion criteria, age, and IQ, and functional correlates have rarely been assessed.

Objectives: To compare TBV, gray matter (GM), white matter (WM) volume and mid-sagittal CC area in ASD and typically developing subjects and explore correlations with visuo-motor coordination and imitation abilities.

Methods: TBV, gray matter (GM), and white matter (WM) volume as well as mid-sagittal CC area were compared between 15 medication-naïve high functioning adolescent and young adult ASD subjects and 15 healthy control individuals. In addition, computational surface-based methods were implemented to encode callosal thickness at high spatial resolution. Also, measures on visuo-motor coordination and imitation abilities were assessed.

Results: TBV, GM, and WM were increased, and CC area was decreased in ASD subjects, a finding, which was prevailingly due to ASD subjects with lower IQ. Only in control subjects, positive correlations of IQ with volume measures were observed. In addition, ASD subjects showed reduced thickness in the posterior part of the CC. WM volume was negatively correlated with dynamic balance and imitation abilities across groups.

Conclusions: This study replicates and expands previous structural MRI findings in ASD and adds evidence for functional implications of these structural changes.

105.23 23 Differences in Cortical Thickness in Autism Spectrum Disorders and Relation to Everyday Executive Function. K. M. Mak-Fan*[1], M. J. Taylor[2], M. K. Malone[2], W. Roberts[1] and J. P. Lerch[3], (1)*University of Toronto*, (2)*Hospital for Sick Children*, (3)*The Hospital for Sick Children*

Background: Recent research has suggested that cortical growth follows an abnormal developmental trajectory in children with autism spectrum disorders (ASD), resulting in regional abnormalities in brain volume (e.g., Carper and Courchesne, 2005). These findings may be due to abnormalities in cortical thickness, but only a few published studies have examined this question. In addition, the relation between structural abnormalities and behavioural symptoms of ASD, such as executive function impairment, has also been largely unexplored.

Objectives: To examine differences in cortical thickness between a group of typically developing children and a group of children with ASD, and to explore correlations between cortical thickness and a measure of everyday executive function (the Behaviour Rating of Executive Function (BRIEF), Gioia et al., 2000), skills known to be impaired in children with ASD.

Methods: Participants were 32 typically developing children (mean age 10.2 years, SD= 2.47) and 21 high-functioning children with ASD (mean age 9.72 years, SD = 2.40). T1-weighted MR images were obtained for all subjects on a 1.5 Tesla GE scanner. Cortical thickness maps were derived from these MRI data for each subject as described elsewhere (Lerch and Evans, 2005), and between-group statistical analyses were then performed with mean cortical thickness covaried. We corrected for multiple comparisons were corrected for using the False Discovery Rate (Genovese et al., 2002). Ethical approval for the study was obtained in accordance with the Hospital for Sick Children (Toronto, ON) guidelines.

Results: Mean cortical thickness was greater in the ASD cohort, although this did not reach significance. Between-group analyses revealed thicker cortex for the children with ASD in the posterior cingulate gyrus (0.23±0.05mm, t=4.3, q=0.07) and the parieto-occipital junction (0.26±0.07mm, t=3.9, q=0.08) for the ASD children. These patterns were fairly bilateral, but more pronounced in the right hemisphere.

In children with ASD, preliminary analyses using overall composite scores on the BRIEF suggest that these measures are correlated with differences in cortical thickness in the cingulate gyrus and parieto-occipital junction, dorsolateral prefrontal cortex (DLPFC), temporal pole and premotor cortex. This pattern of correlation, although weaker, was also found for t-scores on BRIEF subscales such as Emotional Control and Shift.

Conclusions: Regional differences in cortical thickness were observed in children with ASD compared to typically developing children between 7-13 years of age, primarily in the cingulate and parieto-occipital areas. There were also trends for cortical thickness in regions important for executive function (e.g. cingulate, DLPFC) to correlate with scores on a behavioural measure of everyday executive function (BRIEF). This relation between structural abnormalities and behavioural symptoms may contribute to the growing understanding of the neurodevelopmental basis of ASD symptoms.

105.24 24 Automatic Classification of Structural MR Scans Using Support Vector Machine: a Diagnostic Tool for Adult Autism?.

C. Ecker*[1], V. Rocha-Rego[2], P. Johnston[1], J. Mourao-Miranda[3], A. Marquand[3], E. Daly[4], C. Murphy[1], D. Murphy[1] and M. R. C. AIMS Consortium[5], (1)*King's College London, Institute of Psychiatry*, (2)*University of Rio de Janeiro*, (3)*Centre for Neuroimaging Sciences*, (4)*Institute of Psychiatry, King's College London*, (5)*Institute of Psychiatry*

Background: Autistic spectrum disorder (ASD) is a highly genetic neurodevelopmental disorder, which is characterized by impairments in social communication, social reciprocity, and repetitive behaviour. Although autism is accompanied by significant differences in brain anatomy, it continues to be diagnosed on the basis of behavioural criteria. Additional biologically based methods may, however, aid the diagnosis; but this has not previously been tested.

Objectives: The aims of this study was to investigate the diagnostic value of grey matter anatomical images in adults with ASD.

Methods: Support Vector Machine algorithms (SVM) were used to automatically classify structrual MRI scan in a sample of 54 male adults; 27 with a diagnosis of ASD made using gold standard research interviews and 27 healthy matched controls. The performance of the classification was evaluated using the leave-two-out cross validation approach. To identify the degree to which the classification is driven by autistic symptoms, the test marging was correlated the level of symptom severity.

Results: SVM correctly classified individuals with autism based on their grey matter anatomy with 67% specificity and sensitivity. The test margin (i.e. distance from separating hyperplane) was positively correlated with the level of symptom severity as measured by the Autism Spectrum Quotient (AQ) and Autism Diagnostic Observation Schedule (ADOS) The most discriminating regions between groups were the (1) the limbic system, (2) the fronto-striatal system, and (3) fronto-temporal and fronto-parietal networks. In addition, we found increased regional volumes in components of the cerebellar circuitry.

Conclusions: The brain regions identified by SVM are in agreement with many previous studies employing voxel-based analyses, and have been functionally linked to autistic core symptoms in the past. In addition we have shown that the classification was driven by autistic symptoms rather than autism-unrelated effects. Therefore we propose that the application of SVM on grey matter anatomical scans might provide a valid

neuropathological screening tool for ASD to guide and complement a traditional behaviourally guided diagnosis in the future.

105.25 25 A Preliminary Structural Magnetic Resonance Imaging Study of Individuals with Schizotypal and Autistic Traits. A. C. Stanfield*[1], T. W. J. Moorhead[1], M. D. Spencer[2], D. G. C. Owens[1], S. M. Lawrie[1] and E. C. Johnstone[1], (1)*University of Edinburgh*, (2)*University of Cambridge*

Background: Although autism and schizophrenia are usually readily distinguished on the basis of severe impairments in communication skills in the former and the presence of marked positive symptoms in the latter, there exist spectrum forms of these conditions in which this differentiation is less obvious. Individuals with either autism spectrum or schizophrenia spectrum conditions may display social difficulties, bizarre behaviour and idiosyncratic language, as well as a wide range of psychopathology including anxiety, obsessive-compulsive phenomena and mild positive symptoms. As a result, approximately one third of people with an autism spectrum disorder (ASD) meet diagnostic criteria for schizotypal personality disorder and in such cases the primary diagnosis may be unclear. Indeed it is possible that it is incorrect to even regard the spectrums as distinct entities.

Objectives: To identify brain structural features which differ between individuals with schizotypal traits and those with autistic traits.
To examine brain structure in individuals with comorbid schizotypal and autistic traits in order to determine whether it is possible to assign this group to a primary diagnosis.

Methods: Individuals were recruited as part of larger study into the mental health of adolescents receiving educational assistance. Only male participants are considered here as there were insufficient female participants with prominent autistic traits to examine the effects of gender. All participants received the Structured Interview for Schizotypy (SIS) and a structural magnetic resonance imaging scan. In addition, a parent of the child completed the Social Communication Questionnaire (SCQ) along with an investigator. Participants were divided into four groups using cut-offs on the SCQ and the SIS – 'schizotypal', 'ASD', 'comorbid' and 'neither'. Volumes of the cerebral lobes and the cerebellum were derived using automated methods derived in our laboratory and validated against hand tracing (all ICCs > 0.9). Between group differences in volumes were determined using analysis of covariance, with total brain volume as a covariate.

Results: 85 participants were recruited (age range 13-22; IQ range 40-131; SIS range 10-66; SCQ range 0-33). There were no differences in age or IQ between the four groups. The main effect of the ANCOVA revealed a trend towards a difference in left temporal lobe volume between groups ($F=2.28$, $p=0.09$). Between group t-tests showed that the mean left temporal lobe volume in the ASD group was significantly smaller than in the schizotypal group ($p=0.05$) and the comorbid group ($p=0.01$). There were no significant volume differences between the comorbid and the schizotypal groups.

Conclusions: Although preliminary these data indicate that it is possible to differentiate individuals with schizotypal traits from those with autistic traits using brain anatomical measures, supporting the conceptualisation of the schizophrenia and autism spectrums as distinct entities. In addition, individuals with comorbid schizotypal and autistic traits may be more correctly classified as schizotypal. Ongoing work will further investigate these findings using more clearly defined groups.

105.26 26 An Anatomical MRI Investigation of Asymmetries in Frontal and Temporal Language Association Cortex in Children with Autism Disorder. A. L. Isenberg*[1], J. Juranek[2], P. Filipek[1], K. Osann[1], M. A. Spence[1] and N. M. Gage[1], (1)*University of California, Irvine*, (2)*The University of Texas, Health Science Center at Houston*

Background: Recent MRI investigations of volumetric-based hemispheric asymmetries in high functioning children and adolescents with autistic disorder (AD) have provided evidence for abnormal patterns of cortical asymmetry. We used MRI to assess hemispheric asymmetries in frontal and temporal lobe cortical language regions in a large sample of relatively low functioning children with AD to determine if similar patterns of asymmetry are found in younger, lower functioning children.

Objectives: We conducted quantitative morphometric analyses of perisylvian and frontal regions in children with AD to elucidate the relationship between brain structure and language function. Objectives were to (i) assess hemispheric asymmetries in temporal and frontal language association cortex, (ii) determine the correspondence, if any, to neuropsychological

measures of language function, and (iii) evaluate the concordance of these measures in three sets of monozygotic (MZ) twins to examine the role of epigenetic factors.

Methods: Sample: 53 children (44 male), ages 2-14yrs, who met ADOS and ADI-R research criteria, including three pairs of MZ twins (one of each pair was randomly excluded from the larger sample). Segmentation and cortical parcellation was performed on anatomical MRI images as previously described (Filipek et al., 1994). Regions of interest (ROIs) were planum temporale (PT) and posterior Superior Temporal Gyrus (pSTG), corresponding to the functional region Wernicke's area, and pars triangularis (F3t) and pars opercularis (F3o), corresponding to the functional region Broca's area. Comparisons of volume were calculated and expressed using a symmetry index (SI=(2*(L-R))/(L+R)), positive numbers indicate a leftward preponderance. Neuropsychological measures (verbal IQ [vIQ], PPVT) were collected to determine their correspondence to lateralization in cortical language areas.

Results: Full sample (n=50): rightward asymmetry in temporal regions: pSTG (mean SI=-.0114, p<.01), PT showed a rightward, non significant, trend (mean SI=-.061, p=.08). PT and pSTG SIs were positively correlated (r=.444, p<.01). Frontal regions: no significant asymmetries observed. When we constrained the sample to right-handed boys (n=30), direction of asymmetry results did not change. Temporal regions: pSTG (mean SI=-.145, p<.01), PT (mean SI=-.094, p<.05). SIs for PT and pSTG were positively correlated (r=.404, p<.05). Frontal regions: no significant asymmetries observed. SIs for F3t and F3o were positively correlated (r=.414, p<.05). The full sample F3t SI showed a weak positive correlation with vIQ, that was significant when the sample was constrained to right-handed boys (r=.418, p<.05). PT asymmetry was age dependent, with greater rightward asymmetry as a function of age. We also report lack of concordance for asymmetry in frontal and temporal language association cortex in a cohort of MZ twins.

Conclusions: Findings of atypical rightward asymmetries in PT and pSTG, suggest a relationship in the maturational path of these two temporal lobe language regions. Variability between subjects contributed to non-significant asymmetries in the two frontal lobe regions; however they were significantly correlated within subject, providing further evidence for similar developmental paths. The correlation pattern reflecting higher vIQ scores associated with more typical, leftward asymmetry in F3t demonstrates a tentative link between anomalous brain structure and functional impairment. MZ twin results indicate epigenetic factors are involved in the development of cortical language association regions.

105.27 27 Anatomical Landmarks Based Analysis of the Corpus Callosum Abnormalities in Essential Autism. Y. Duan*, Q. He, K. Karsch and J. H. Miles, *University of Missouri*

Background:

Brain MRI studies has reported inconsistent results regarding the abnormalities of brain structures in autism. The inconsistency may be due to factors such as the sample size, subject age and gender. However, heterogeneity within the autism diagnosis can significantly obscure the genetic basis of the disorder. Recently, we proposed a new definition of autism subgroups, which divided autism into essential autism and complex autism. Essential autism comprises the majority of patients and includes the more heritable segment of autism compared to complex autism, and a higher male to female ratio. Complex autism, on the contrary, shows more heterogeneous features such as lower IQs, more seizures, and poorer outcomes, etc.

Objectives: The aim of this study was to identify shape differences of the corpus callosum, the major commissural pathway between the brain hemispheres, between patients with essential autism and the controls using anatomical landmarks extracted from the corpus callosum (CC). We limit our subjects to essential autism group in order to rule out as much as within-group heterogeneity which can lead to inaccurate statistical findings in the brain morphology analysis.

Methods:

Euclidean Distance Matrix Analysis (EDMA) and Thin-plate spline (TPS) are two traditional approaches to analyze the landmarks. EDMA uses landmark coordinate data to calculate all pairwise distances between landmarks. It is invariant to the coordinate system, which makes it biologically

and statistically advantageous. TPS has been widely used to compare landmark configurations. The fundamental principle of TPS is the comparison of two different shapes by deforming one shape to the other. The deformation requires bending energy, which can be analyzed in terms of partial warp (PW) scores. Analysis of covariance is performed to compare the group mean PW scores.

Although the above landmark analyses can reveal some shape information, local shape morphologies at non-landmark locations cannot be detected. In this paper, we examine the abnormalities of the CC in essential autism by integrating the traditional landmark analyses with a landmark guided local shape comparison. A configuration of landmarks is identified in brain MRI mid-sagittal sections based on a predefined criterion. In the traditional analyses, we perform the aforementioned EDMA and TPS procedures. In the landmark guided shape comparison, we aim at finding the morphology at every location on the shape. Point correspondence is established locally based on the landmark correspondences, and statistical methods are used to compare two groups of shapes (essential autism vs. control) at every location. Each of the three analyses examines the shape morphology from a different perspective.

Results:

Brain MRIs of 30 essential autistic patients and 24 controls are studied. The results revealed significant form difference in the landmarks between patients and controls. The corresponding pairwise distances that caused the form difference were found in anterior and posterior of the CC. No influence of the size or the diagnosis on the shape deformation was found, but a reduced centroid size of the CC in patients was found.

Conclusions:

We proposed a new landmark based shape analysis method and the result is consistent with previous studies.

105.28 28 Age-Related Differences in White Matter in Children and Adolescents with Autism. G. M. McAlonan*, V. Cheung, C. Cheung, N. Wong and S. Chua, *University of Hong Kong*

Background:

Abnormalities in white matter circuits are implicated in autism. White matter maldevelopment may drive the dramatic changes in brain volume in young children and in older children and adults, and structural or functional MRI datasets suggest widespread disconnectivity. The period of development from childhood into adolescence is marked by heterochronous brain changes in typically developing individuals which parallel maturation of cognitive and emotional abilities. However, the trajectory of age-related changes in white matter from childhood into adolescence is not well known.

Objectives: To map age-related differences in white matter in children and adolescents with autism aged between 6 and 16 years old.

Methods:

T2/PD scans were acquired from children with ASD (n = 36) and typically developing controls (n = 55) group matched for age, gender, ethnicity and handedness. Diffusion Tensor Imaging (DTI) scans were acquired from a subgroup of participants. Voxel based morphometry (VBM) was used to map age-related changes in white matter volume in both groups. The age-volume maps from each group were overlaid and used to define 'regions-of-interest' (ROI) for DTI analysis in a subgroup of children. Fractional anisotropy (FA) values and correlations between age and FA in these ROI were examined.

Results:

There was a positive correlation between age and white matter volumes in ventral frontal lobe in controls only. There was a negative correlation between age and cerebellar white matter volume in the autism group only. There were positive correlations between age and white matter volumes throughout parietal, occipital and dorsal frontal lobe in both groups, as between age and FA in these regions. There was a significant positive correlation between age and FA in the ventral prefrontal lobe and left internal capsule of the control group, not the autism group. There were no age-related changes in FA in the cerebellum of either group.

Conclusions:

The antero-posterior gradient of brain maturation is disrupted in autism. This study indicates

dysmaturation of frontal and cerebellar pathways in autism with relative sparing of posterior hemisphere systems in autism. Given the joint roles of cerebellum and frontal lobe in cognitive and social functioning, this disordered development likely makes a major contribution to persistent symptoms in autism.

105.29 29 Myelin Imaging in Autism - Preliminary Reports. J. Zinkstok*[1], E. Daly[2], C. Ecker[3], P. Johnston[3], D. Murphy[3] and S. Deoni[2], (1)*Institue of Psychiatry, King's College London*, (2)*Institute of Psychiatry, King's College London*, (3)*King's College London, Institute of Psychiatry*

Background: Autism is a pervasive developmental disorder characterized by social, communicative and behavior impairments. A hypothesized substrate of the disorder is aberrant white matter maturation and abnormal myelination, evidence of which has been suggested by volumetric, spectroscopic and diffusion tensor magnetic resonance imaging studies. However, while these methods provide *qualitative* information *related* to white matter microstructure and fiber coherence, they do not *quantitatively* evaluate myelin content, which is believed to underlie the observed white matter changes. Multi-component Driven Equilibrium Single Pulsed Observation of T_1 and T_2 (mcDESPOT) is a recently proposed magnetic resonance imaging (MRI) method which allows whole-brain myelin analysis. With mcDESPOT, the MR signal is decomposed into contributions from water in the intra- and extracellular compartments, and water trapped between the lipid layers of the myelin sheath, allowing quantification of each compartment's volume fraction. These measures of myelin water content correlate strongly with histological myelin assessments. Here we report on a pilot study comparing myelin content throughout the brain in people with Autism Spectrum Disorders (ASD) and healthy controls using mcDESPOT.

Objectives: To *quantitatively* compare myelin content in people with ASD and healthy controls using the mcDESPOT multi-component relaxometry MR imaging method.

Methods: To date, *in-vivo* data from 14 healthy male controls (aged 23-36) and 2 male autism spectrum disorder (ASD) patients (aged 25 and 26) right-handed, of normal intelligence (IQ>70) and not using medication, have been collected. Following acquisition, mcDESPOT analysis, and normalization to standard MNI space, voxel-wise maps of mean myelin content (and standard deviation) were calculated from the healthy volunteer data. To investigate differences in the ASD patients, Z-scores were calculated voxel-wise and thresholded to identify areas of substantial difference (Z +/- 4). Mean values were then obtained from regions of interest (ROIs) placed within identified areas.

Results: Preliminary results suggest that ASD patients have reduced myelin content bilaterally within the frontal lobe and internal capsule. This myelin reduction in the frontal lobes is consistent with prior reports of white matter volume reductions in these areas, suggesting variations in myelin content may underlie these established observations. From the ROI analysis, healthy population myelin volume fraction values obtained for the right and left frontal lobes were: 24.1 (0.002)% and 23.6 (0.0017)%, respectively, and for right and left internal capsule: 21.3 (0.009)% and 22.6 (0.0019)%, respectively. For ASD patient #1, corresponding values were: 23.4 (0.012)%, 23.9 (0.01)%, 22.2 (0.014)% and 21.1 (0.009); and for ASD patient #2: 20.2 (0.011)%, 20.9 (0.009)%, 19.2 (0.015)% and 18.9 (0.007)%.

Conclusions: Though preliminary, these results attest to the investigative potential of the mcDESPOT approach in ASD. While aberrant myelination has been proposed to underlie ASD symptoms, to date this hypothesis has been difficult to directly test due to the absence of a suitable myelin imaging technique. Our method, reported here for the first time, provides a new quantitative technique for measuring brain myelination in people with autism.

105.30 30 White Matter Integrity and Volumetrics in the Investigation of Structural Connectivity in School-Aged High Functioning Boys with ASD. N. Shetty* and M. Herbert, *Massachusetts General Hospital*

Background: Given the frequent replication in ASD research of the findings of large brains, increased white matter and of atypical connectivity, it is important to investigate the nature and distribution of the tissue changes that may be contributing to these observed abnormalities.

Objectives: Our goal is to investigate white matter structural integrity in a well-characterized cohort using MRI methods to quantitate water diffusion properties, and to assess the relationship of these findings to neurocognitive phenotypic features.

Methods: High resolution Diffusion MRI and 1mm isotropic T1-weighted MPRAGE scans were acquired using a 3T Siemens scanner on high-functioning 6-13 year olds with Autism Spectrum Disorder and age matched typically developing children.
Analytical methods include Voxelwise statistical analysis performed using FSL's Tract Based Spatial Statistics (TBSS) tool and volume-based analyses using Freesurfer and manual volumetric analysis using segmentation and parcellation techniques from the Center for Morphometric Analysis at MGH. TBSS was used to localize areas where group differences in white matter Fractional Anisotropy and Mean Diffusivity show significant differences. Volumetric methods were then used to further quantify characteristics of regions with altered white matter properties.
Results: Preliminary results indicate some differences in the measured DTI metrics, which will be presented in relation to whole-brain volumetric and neurocognitive data.
Conclusions: The use of several coordinated macroanatomic methods to assess white matter alterations in ASD is important for sharpening hypotheses about underlying microanatomic alterations contributory to abnormal connectivity.

105.32 32 A Diffusion Tensor Imaging Study of the Social Brain in Autism. L. Poustka*[1] and B. Stieltjes[2], (1)*Central Institute of Mental Health*, (2)*German Cancer Research Center, Germany*

Background: It is hypothesized functional underconnectivity between regions comprising the mentalizing network contribute to the social impairments in autism, especially in the earlier cerebral development. Aspects of the orbital and medial prefrontal cortices, the amygdala and lateral aspects of the temporal cortex are target regions for the so called social brain.

Objectives: To investigate structural integritiy of white matter tracs in austistic children

Methods: Diffusion tensor imaging (DTI) was performed on 20 autistic children and 20 healthy controls aged 6-12 years matched for age, sex, handedness and IQ. We examined the structural connectivity of key regions of the mentalizing network using DTI and volumetric measures. In addition, fractional anisotropy (FA) values were correlated with symptom severity as indexed by the children's scores on the Autisms Diagnostic Observation Schedule (ADOS) and the Autism Diagnostic Interview-Revised (ADI-R).

Results: Results showed that there were significant differences of FA values between groups. Additionally, low FA values were inversely related to children's ADOS and ADI scores in social interaction and communication, but not in the domain of repetitive and stereotypic behaviour.

Conclusions:

In summary, reductions in the structural integrity of white matter in autism are observable in young autistic children and may contribute to social and communication deficits of the disorder.

105.33 33 Diffusion Tractography of Frontal and Temporal Lobe Pathways to the Amygdala in Adolescents with Autism Spectrum Disorders. M. Carrasco*, J. L. Wiggins, S. J. Weng, S. Peltier, S. Perkins, K. Fitzgerald, C. Lord and C. S. Monk, *University of Michigan*

Background: Research has shown that the amygdala plays a central role in the socioemotional processing of faces. Differences in anatomical connectivity between the amygdala and brain structures involved in face and emotional perception may be responsible for some of the social deficits encountered among individuals with Autism Spectrum Disorders (ASD). Studies focusing on anatomical connectivity in ASD between the amygdala and its frontal and temporal projections have been limited; our study will aim to address this gap in the literature.

Objectives: We used diffusion tensor imaging (DTI) to estimate regional white matter properties in ASD and typically developing participants. Group differences were assessed in the projections between the amygdala and the medial frontal/orbitofrontal cortices, and the amygdala and medial temporal cortex structures.

Methods: Our preliminary sample includes 7 ASD and 10 controls; final analyses will be performed once 15 ASD and 15 controls have been recruited. ASD and control subjects were equivalent for IQ, age (range 11-17), sex, and manual preference. In addition, ASD adolescents were diagnosed using the ADOS and ADI-R and the diagnosis was confirmed by clinical consensus. For diffusion tensor image analysis, a diffusion weighted single-shot spin echo-planer imaging (DWSSEPI) sequence acquired 34 axial slices to cover the regions of interest, with a TE/TR of 90/6500 ms, a matrix of 128x128, an FOV of 220 mm, a slice

thickness of 2.5 mm, and 6 averages. Diffusion weighting was applied in 12 directions with a b-value of 1000 s/mm2. The diffusion tensor was calculated for each voxel, and averaged diffusion coefficient (ADC) and the fractional anisotropy (FA) maps were generated. After transformation to a common anatomical space, fractional anisotropy image values were used as measures in a two-way ANOVA.

Results: Preliminary results show group differences in fractional anisotropy (FA) within the left amygdala. FA values were higher in adolescents with ASD relative to controls (MNI coordinates at center of cluster: x = -19, y = -4, z = -24; cluster 91; t value = 6.57). Tractography analyses will focus on group differences in amygdala projections to the medial frontal/orbitofrontal cortices and to neighboring medial temporal structures.

Conclusions: Preliminary results show group differences in white matter properties within the left amygdala. Upcoming tractography analyses will yield additional information on the anatomical connections between the amygdala and frontal/temporal structures involved in socioemotional face processing in ASD adolescents.

105.34 34 Amygdala Activation in Response to Configural and Featural Facial Changes in ASD. J. D. Clark*, C. R. Corbly, M. Huffman, M. Wheatley, L. A. Ruble, R. S. Bhatt, P. Glaser and J. E. Joseph, *University of Kentucky*

Background: Autism Spectrum Disorder (ASD) is characterized by deficits in social communication including an impaired ability to extract emotional and perceptual information from faces. Non-diagnosed siblings of individuals with ASD (ASD-sibs) share some less severe characteristics of autism including mild deficits in face perception. Whether these face processing deficits are due to a bias to process faces in a piecemeal, locally oriented fashion or due to impaired ability to process global information in faces remains in dispute. At present, the neural substrates of impaired face processing in ASD are not fully understood. For example, the fusiform face area (FFA) does not show strong activation to unfamiliar faces, but does show activation when face stimuli are relevant (Pierce et al., 2008). Amygdala abnormalities are widely reported in ASD during tasks involving emotional face discrimination (Golarai et al., 2006; Schultz, 2005). In typically developing (TD) individuals, the amygdala responds to configural and featural aspects of fearful faces (Morris, 2002). However, a possible role of the amygdala for featural and configural face processing in ASD remains unexplored.
Objectives: Using fMRI, we explore whether amygdala function for featural and configural face processing differs between ASD and ASD-sibs.
Methods: Participants enrolled thus far include five ASD children (mean age = 12) and five ASD-sibs (mean age = 13.5). During a block design fMRI task, subjects indicated via button press whether two images (either houses or faces) presented side by side were the same or different. Functional runs consisted of two blocks each of featural changes to faces (FF) or houses (HF) or configural changes to faces (FC) or houses (HC). Within each block two same and four different pairs were presented. fMRI data were analyzed using FMRIB's FSL package. After standard preprocessing and individual-subject level statistics, preliminary analyses of each group (ASD and ASD-sibs) were conducted. The main contrasts of interest were: FF vs. HF, FC vs. HC, and Faces vs.
Houses.

Results:
Behavioral results indicate that both groups of children performed the task well. Preliminary fMRI results indicate that the ASD group showed significantly greater activation of the right amygdala for configural face versus configural house processing, but greater left amygdala activation for featural face versus featural house processing. ASD-sibs did not show this differential response of the amygdala to faces. However, ASD-sibs activated a region consistent with the right fusiform face area (FFA) during face versus house blocks but the ASD group did not.
Conclusions: Preliminary results are consistent with other studies showing either reduced or no right FFA activation for unfamiliar faces in ASD individuals across a variety of face processing tasks. The present findings of greater amygdala activation in ASD subjects compared to ASD-sibs suggest that this region may play a role in the development of configural face processing. Moreover, whereas Morris et al. (2002) found left amygdala recruitment for configural aspects of faces in TD individuals, we find the right amygdala is responsive to configural processing in

ASD. Future work will include comparisons with age-matched typically developing controls.

105.35 35 Multisensory Integration of Visual and Vocal Emotional Cues in Autism. K. M. Dalton* and R. J. Davidson, *University of Wisconsin*

Background: : Adaptive social functioning requires exquisite integration of multiple environmental cues both automatically and attentively. Deficits in multisensory integration can lead to poor or incorrect causal references in relation to linked environmental cues. It is proposed that deficits in social/emotion processing associated with autism are related to poor multisensory integration of external emotional cues and have their basis in cortical and subcortical dysfunction in areas associated with social/emotional processes and multisensory integration.

Objectives: The aim of this study was to investigate unisensory auditory prosody processing and multisensory integration of visual and auditory emotional cues and underlying brain activation patterns and physiological and behavioral sequela associated with these processes in autism.

Methods: A sample of 17 male and 6 female (age: M = 15.5, SD = 4.9) individuals with a diagnosis of autism spectrum disorder (ASD) participated in the study. A sample of 17 male and 6 female (age: M = 13.26, SD = 3.91) of typically developing (TD) individuals served a comparison group. Brain functional images were acquired while participants performed an event related facial emotion discrimination task. Images of emotional human faces and audio clips of emotional voices were presented simultaneously in the MRI scanner. The emotional expression of the face was crossed with the emotional prosody of the voice to produce 4 multisensory conditions. Participants were asked to judge the emotional facial expression by pressing one of two buttons. Participants were also asked to identify the emotional prosody of the voices in a separate task in the scanner.

Results: he TD group performed significantly better (M = 97.4%) on the emotional face identification task compared to the ASD group (M = 87.8%; p = .016). The ASD group had marginally longer reaction times (RT) across all the conditions (M = 1758.1s, SD = 566.4) compared to the TD group (M = 1533.8, SD = 394.9; p = .09). Interestingly, the ASD group also displayed significantly longer RTs to the incongruent vs. congruent trials (p = .03). This effect was not found in the TD group. The TD group also performed significantly better (M = 90.3%) on the emotional prosody task compared to the ASD group (M = 75.9%; p = .002). The ASD group spent significantly more time per trial fixating the mouth region across all trials (M = 203ms, SD = 177.97) compared to the TD group (M = 107.18ms, SD = 98.87; p=.018). The ASD group had lower HRV during the faces plus voices task (M = 6.58, SD = 1.07) compared to the TD group (M = 7.43, SD = 0.93; p = .009). Analyses of the brain functional data and the relationship between brain and behavioral measures are in progress and will be presented.

Conclusions: While the ASD group performed the emotional face recognition and emotional prosody recognition task above a chance level, as a whole, their performance was statistically below that of the TD group. These performance measures may be related to brain and peripheral physiological differences in the ASD vs. TD group.

105.36 36 Visuomotor Interhemispheric Information Transfer in Autism. E. B. Barbeau*[1], L. Mottron[1], A. Mendrek[2] and T. A. Zeffiro[3], (1)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (2)*Centre de Recherche Fernand-Seguin, Université de Montréal*, (3)*Neural Systems Group, Massachussetts General Hospital*

Background: It has been widely speculated that autism is associated with an atypical state of regional integration, the mechanism by which spatially separated neural processing centers exert mutual influences. This notion has gained support from the growing evidence of atypical white matter microstructural integrity in autistics involving the pathways underlying both intra- and inter-hemispheric information transfer. This evidence of atypical structural connectivity suggests that tasks requiring information transfer among widely distributed neural processing centers would be associated with detectable behavioral differences when comparing autistic and non-autistic samples performing tasks engaging processing centers in both hemispheres.

Poffenberger was the first to demonstrate that the simple reaction time (RT) to a stimulus presented laterally in the visual periphery is faster when the principally involved visual and motor cortical areas are in the same hemisphere than when they are in opposite hemispheres. Since then, there have been numerous studies utilizing this paradigm to study the mechanisms of interhemispheric

information transfer. The task is used specifically to derive measures of the inter-hemispheric transfer time (IHTT) by comparing task conditions requiring interhemispheric transfer to those that do not.

Objectives: Our goal was to determine whether autistics would exhibit atypical performance on the Poffenberger task, consistent with the notion that atypical structural connectivity would be associated with atypical IHTT.

Methods: We compared groups of autistics and non-autistics, matched on IQ, sex and age. The task was a simple reaction time paradigm requiring responses to lateralized visual stimuli collected over the course of 600 trials. The IHTT was estimated from differential response timing (with the right or the left hand) following presentation of brief visual stimuli in the left or right lateral visual field, reflecting the additional time needed for the information to move among the participating regions.

Results: The mean simple response time did not differ significantly between groups. Within groups, there was no difference in the mean response time grouped by response hand or visual field. However, the estimated IHTT was found to be significantly different in the autistic and non-autistic groups, with the autistic group exhibiting lower IHTTs and much higher IHTT variability.

Conclusions: The reduced and more variable IHTT in the autistic group is consistent with the characterization of autism as a state of atypical regional functional integration. While the autistic and non-autistic groups performed the task with equivalent overall speed and accuracy, the task conditions requiring information transfer between the hemispheres were associated with more variable performance in the autistic group, suggesting that underlying developmental differences in white-matter microstructure might result in autistics adopting different processing strategies when confronted with tasks that require transmission of sensory information from one hemisphere to motor control systems in the opposite hemisphere.

105.37 37 High- Vs. Low-Level Perceptual Processing in Autism: An fMRI Study. Y. Liu*, V. Cherkassky and M. A. Just, *Carnegie Mellon University*

Background:

Behavioral evidence suggests that low-level visual-spatial processing may be preserved or enhanced in autism. On the other hand, the capacity of individuals with autism to process high-level complex stimuli like faces is impaired. Theories have been proposed to interpret the discrepancy in performance in autism between low-level and high-level complex visual perceptual tasks. Investigation of the brain mechanisms, including brain activation as well as functional and anatomical connectivity underlying this discrepancy may lead to further understanding of the cognitive processing associated with the behavioral disorder of autism.

Objectives:

This fMRI study compares the behavioral performance, brain activation, and cortical synchronization in individuals with autism and healthy controls when they perform a low-level line counting task and a high-level possibility judgment of 3-D figures.

Methods:

In the experiment, participants with high-functioning autism (HFA) and age/IQ-matched healthy controls see possible and impossible 3-D figures. In the possibility judgment condition, participants are presented with a single figure to be judged as possible or impossible to be constructed in three dimensions; in the line counting condition, red and green lines are drawn on a possible or impossible figure and participants are asked to count and decide whether there are more red or green lines. To date, data have been collected on 8 adults with HFAs and 14 typically developing age and ability-matched controls. Data collection is on-going.

Results:

It is anticipated that the behavioral performance of the individuals with autism on the possibility judgment task will be worse (e.g., slower reaction times and lower accuracy), and that they will show lower functional connectivity between frontal regions and more posterior regions than healthy controls. On the other hand, their cognitive ability in the line counting task will be preserved or enhanced. The autism group may show normal or even enhanced functional connectivity among posterior regions associated with perceptual

processing. The behavioral performance on the collected individuals is consistent with the expected pattern. The fMRI data analysis is on-going.

Conclusions:

If the results are as expected, it will suggest that high-level complex perceptual tasks may require the coordinated functioning of the frontal-posterior system, which is underconnected in the autism. Instead low-level perceptual tasks that do not demand a lot of frontal input are preserved in autism.

105.38 38 Trustworthiness Judgments in Autism: An fMRI Study. S. E. Schipul*[1], D. L. Williams[2], T. A. Keller[3], N. J. Minshew[4] and M. A. Just[3], (1)*Center for Cognitive Brain Imaging, Carnegie Mellon University*, (2)*Duquesne University*, (3)*Carnegie Mellon University*, (4)*University of Pittsburgh School of Medicine*

Background: Previous studies have shown that individuals with autism spectrum disorder (ASD) do not judge faces for trustworthiness in the same way that neurotypical individuals do. Adolphs, Sears, & Piven (1998 & 2001) reported that individuals with ASD rated the least trustworthy faces as more trustworthy than neurotypical participants did. Interestingly, they found this same effect in individuals with amygdala brain damage. However, when participants rated written biographies, the authors found no difference between neurotypical participants and participants with ASD or amygdala damage patients, suggesting these atypical trustworthiness judgments are limited to faces. Thus, there appears to be a dissociation in the ability of individuals with ASD to judge faces or context for trustworthiness.

Objectives: This fMRI study investigated the neural activity of high functioning individuals with ASD and neurotypical individuals while they made trustworthiness judgments based on context information and face processing.

Methods: Participants are high-functioning adults with ASD and age and IQ matched neurotypical participants. Participants viewed a face on a computer for 3 seconds and had to answer yes or no to the question, "Would you trust this person?" They then read a story about the person and again saw the face for 3 seconds. Then they decided a second time if they would trust that person. Half the faces were trustworthy and half were untrustworthy, as judged by neurotypical participants in a preliminary ratings task. In half the stories, the reported actions of the character are positive (trustworthy) and in the other half, the actions of the character are negative (untrustworthy). The participants performed the task in a 3T Siemens Allegra functional magnetic resonance imaging scanner.

Results: The behavioral, functional imaging, and functional connectivity data from approximately 15 adults with ASD and 15 matched neurotypical adults will be presented.

Conclusions: It is anticipated that participants with ASD will make use of written context, but not visual information from faces, to judge trustworthiness, while neurotypical participants will use both types of information. It is predicted that this task will recruit activation in the Theory of Mind (ToM) network, including prefrontal cortex, right temporal parietal junction, the superior temporal sulcus, the fusiform gyrus, and the amygdala. It is also predicted that the individuals with ASD will recruit these areas to a different extent than the neurotypical participants. Furthermore, it is expected that neurotypical participants will activate the amygdala more when viewing untrustworthy faces as compared to trustworthy faces, but participants with ASD will not show this difference. Finally, we expect to find differences between our two groups in the functional connectivity between frontal areas and posterior areas while performing this task. These results will provide insight into the abilities of individuals with ASD to make trustworthiness judgments based on visual features of faces and context information. Furthermore, these results will illuminate the neural correlates underlying the differences between individuals with ASD and neurotypical individuals while performing trustworthiness judgments.

105.39 39 Lack of Emotion Modulation of Brain Activation during Face Processing in ASD. R. C. M. Philip*, A. C. Stanfield, J. Hall, H. C. Whalley and S. M. Lawrie, *University of Edinburgh*

Background:

When investigating the neural substrate of the social deficits in ASD, many studies have looked at brain activity in response to face stimuli. Whilst many of these often include both emotional and neutral stimuli, it is often unclear whether aberrant brain activation in the ASD group is attributable to deficits in face processing, emotion processing or both.

Objectives:

We sought to isolate emotion processing and investigate its neural underpinnings in both neurotypical individuals and those with ASD.

Methods:

Participants: The ASD group consisted of 12 men with a clinical diagnosis of Asperger's Syndrome (8) or autism (4) in accordance with DSM-IV criteria. The ASD group had a mean age of 36.1 years (s.d. 11.8). The control group was matched by age, gender and handedness and consisted of healthy volunteers with no personal or family history of major psychiatric disorders. All study volunteers provided informed consent and the study was approved by the Local Research Ethics Committee.

Task: 6 blocks of static Ekman face stimuli were presented, three blocks expressing prototypical fear and three blocks of faces with neutral expressions. Blocks were interspersed with baseline visual fixation. Participants responded by button press to the presentation of each stimulus.

Scanning: Participants were scanned on a GE 1.5T Signa scanner at the SHEFC Brain Imaging Research Centre, Edinburgh. Functional scans comprised EPI sequence to acquire 99 volumes, TE 40ms, TR 2.5s. Interleaved axial slices were acquired AC-PC aligned with a thickness of 5mm with no gap and matrix size of 64 x 64.

Analysis: Image analysis was conducted using standard techniques in SPM5.

Results:

When blocks of fearful faces were contrasted with neutral faces, the control group significantly activated bilateral inferior parietal lobe and also a region of the middle frontal lobe bilaterally. There were no areas of significant activation in the ASD group. A between group contrast revealed a significant difference between groups in both the left and right inferior parietal lobe, ($p=0.004$ and $p=0.01$ corrected).

Conclusions:

The results indicate that the ASD group fail to respond to the emotional content of face stimuli. This suggests that there is a lack of neural modulation in response to emotion in ASD and this cannot be fully accounted for by a deficit in face processing.

105.40 40 Functional Connectivity of the Somatosensory Cortex during Face Perception in Autism. N. R. Zürcher*[1], B. L. Russo[1] and N. Hadjikhani[2], (1)*Swiss Federal Institute of Technology (EPFL)*, (2)*Swiss Federal Institute of Technology (EPFL) and Harvard Medical School*

Background: Facial mimicry plays a role in emotion recognition and may involve the mirror neurons system (Oberman et al. 2007). There are evidences for deficits in automatic mimicry of emotional facial expressions in autism (McIntosh et al., 2006). Additionally, adults with high functioning autism spectrum disorder (ASD) exhibit decreased activation in the somatosensory cortex and in motor areas corresponding to the face during naturalistic face perception (Hadjikhani et al., 2007). The somatosensory cortex is crucial for emotion recognition (Addolphs et al, 1996), and cortical thinning has been observed in that area in adult ASD subjects (Hadjikhani et al., 2006).
Objectives: The aim of the study was to examine functional connectivity of the somatosensory cortex during naturalistic face perception in high-functioning ASD adults compared to controls.
Methods: 10 ASD subjects: 7 males; 24.9 ± 7.6 years (mean ± SD) and 10 age-matched controls: 7 males; 27.8 ± 8.1 years underwent anatomical and functional scanning on a Siemens 3T Tim Trio scanner. Visual stimuli consisted of grayscale pictures of naturalistic faces and their own Fourier scrambled version. Participants were instructed to fixate a cross in the center of the stimuli and to perform a one-back task. A functional connectivity analysis was conducted using the FMRIB software library. The somatosensory cortex was selected as the region of interest using the Harvard-Oxford cortical structural atlas. Timecourses were extracted from the peak of the region of interest at an individual level and used as a regressor. Group comparison of connectivity was performed using an unpaired t-test ($p<0.005$).
Results: Preliminary results show that controls have stronger connections between the somatosensory cortex and bilateral motor, premotor and supplementary motor areas, as well as with the inferior frontal cortex, the inferior parietal cortex and the superior temporal sulcus. In addition, stronger connectivity was found in the controls with the pulvinar nucleus of the thalamus and the colliculi. Posterior insula, hippocampi,

temporal gyri and prefrontal cortices also had stronger connectivity with the somatosensory cortex in controls. Finally, controls had stronger correlations between the somatosensory cortex and bilateral visual cortices.
Conclusions: The findings suggest that emotion perception difficulties in ASD are reflected by a decreased connectivity of the somatosensory cortex with motor, premotor and supplementary motor cortices, areas of the mirror neurons system, the visual cortex, as well as with other areas involved in emotion perception and social cognition.

105.41 41 Neural Underpinnings of Prosody Processing in Autism. I. M. Eigsti*[1], J. Schuh[1], E. Mencl[2], R. T. Schultz[3] and R. Paul[4], (1)*University of Connecticut*, (2)*Haskins Laboratories*, (3)*Children's Hospital of Philadelphia and the University of Pennsylvania*, (4)*Yale University School of Medicine*

Background: Prosody, defined as changes in the pitch (fundamental frequency), intensity (amplitude), and duration of speech, is central to the deficits in social communication that characterize individuals with autism spectrum disorders (ASD). Despite its clinical significance, the comprehension of prosody has not been extensively investigated using structured empirical designs. Furthermore, little is known about the neural mechanisms that underlie this important communicative cue. Objectives: This study aims to illuminate the mechanisms that underlie the perception of prosodic cues to both grammatical and emotional qualities in speech. Methods: Adolescents with ASD (n = 4 to date, ages 9 -17 years) and age-, gender-, FSIQ-, and CELF core language-matched typically developing controls (TD; n = 4) completed a implicit prosody perception task while their brain activity was recorded using functional magnetic resonance imaging (fMRI). Prosodic stimuli included emotional (angry, neutral) and grammatical (question, statement) versions of semantically simple sentences (e.g., It is five oclock; She is typing fast). Participants gave a yes/no response, judging whether each sentence was about a living creature; thus, their explicit task was to make a semantic judgment about the sentence. Prosodic sentences were recorded using natural speech, matched on stimulus duration across affective and grammatical manipulations. Statements and questions differed in pitch contour (rising versus falling); angry and neutral stimuli differed in fundamental frequency (high versus medium) and pitch range (large versus medium). Stimuli were presented in 6 runs in a block design, where each run included two blocks of each of the four conditions (emotional prosody: angry X neutral; grammatical prosody: sentences X questions) as well as an auditory attention control task (detecting a beep) and a rest condition. fMRI data were collected at 3.0 Tesla and image processing was performed with BrainVoyager. Results: Behavioral response data indicated that adolescents with ASD were as accurate as controls overall in judging the animacy of stimuli (72% vs. 86%, p = .32). There was a trend towards a group difference in effects of emotional prosody, with sentences in neutral conditions judged less accurately than those in angry conditions by the ASD group (.77 vs. .68, group by condition interaction, p = .09), possibly reflecting a speed/accuracy tradeoff, as the neutral condition response times tended to be shorter. FMRI data suggest a more diffuse and bilateral pattern of activation in response to prosodic contrasts in participants with ASD. In addition, the contrast between emotional prosodic conditions elicited a smaller difference in brain activation for ASD relative to TD participants. Conclusions: This implicit prosody perception task provides a measure of whether participants with ASD engage typical brain networks when passively hearing prosodic cues. While behavioral data indicated that participants were processing the language stimuli with similar attentional engagement, patterns of brain activation suggested a less lateralized pattern of activity in response to acoustic cues to prosody. This difference in neural activity is consistent with previous findings for other language-related tasks, and suggests that brain organization for processes related to language in ASD may be less specialized.

105.42 42 The Role of Temporoparietal Junction in Intentional Causal Attribution in Autism. R. K. Kana*[1], E. R. Blum[1], C. L. Klein[2], L. G. Klinger[2] and M. R. Klinger[2], (1)*University of Alabama at Birmingham*, (2)*University of Alabama*

Background: Attribution of intentions to others, a key element of what is referred to as theory-of-mind, is perhaps one of the most complex forms of human reasoning. Mental state attribution involves the interplay of a set of subprocesses, such as representation of reality, understanding one's own beliefs and the beliefs of others, and taking others' perspective. Understanding the cause and effect of actions is one of the skills that children learn during development. However, individuals with autism are known to have major impairments in the development of intentional causality (Baron-Cohen, 1995; Baron-Cohen et

al., 1985; 1993) whilst having relatively normal or even superior development in their understanding of physical causality (Baron-Cohen, 1997; Frith, 1989; Jolliffe & Baron-Cohen, 1997). The current study investigated this dichotomy in understanding causality and its neural underpinnings in autism.

Objectives: The primary aim of this study was to examine the cognitive and neural mechanisms underlying the attribution of causal explanations to the actions of social and physical agents in individuals with autism.

Methods: Eight high-functioning adolescents and adults with autism and ten age-and-IQ-matched neurotypical controls participated in this fMRI study (data collection in progress). Non-verbal comic strip vignettes involving physical and intentional causal scenarios were presented randomly and the participants had to choose the most logical ending to each vignette. The participants indicated their response by choosing alternatives A, B or C with a button press. The data acquired from a Siemens 3T Allegra scanner were analyzed using Statistical Parametric Mapping (SPM2).

Results: During intentional causal attribution, the performance of participants with autism was significantly poorer with longer response times relative to controls. However, no reliable group difference was found in performance or response time in the physical causality condition. At the cortical level, the underactivation in autism was most pronounced in right superior temporal sulcus at the temporoparietal junction (TPJ), an area associated with theory-of-mind. In addition, the participants with autism also showed reliably lower activation in right inferior parietal lobule, left orbitofrontal cortex and left precuneus. However, no group difference in activation was found in the medial prefrontal cortex (MPFC) while attributing intentional causality.

Conclusions: The findings of this study underscore the impairments in social cognition and theory-of-mind in people with autism, in particular their difficulty in attributing intentions to social agents. Since we did not find any group difference in activation in MPFC in this study, the findings re-ignite the debate about the relative role of temporoparietal junction and medial prefrontal cortex in theory-of-mind. It is possible that the TPJ might be playing a critical role in reasoning about the representational mental states of the character (Saxe and Kanwisher, 2003; Saxe et al., 2006). Functional and effective connectivity analyses are in progress, the results of which might provide more information on the communication between MPFC and TPJ and also the relative functions of each of these regions.

105.43 43 Activation/Inhibition and Autism Versus Asperger Disorder. A. P. Inge*[1], C. Schwartz[2], N. Zahka[3], N. Kojkowski[3], D. Coman[3], L. Mohapatra[3], C. Hileman[3], H. A. Henderson[3] and P. C. Mundy[4], (1)*University of North Carolina School of Medicine*, (2)*Yale University*, (3)*University of Miami*, (4)*UC Davis*

Background: The diagnosis of High Functioning Autism (HFA) versus Asperger's Disorder (AD) is based on language impairment, but the utility and validity of this distinction remains controversial. Alternatively these subgroups may differ on the motivational continuum for approach versus avoidance behaviors regulated by the Behavioral Activation System (BAS) and the Behavioral Inhibition System (BIS). Specifically, we have raised the hypothesis that a predisposition to Behavioral Activation may lead individuals with Autism Spectrum Disorders (ASD) to engage in more interactions, be more active and effective in early language learning, be harder to diagnose early in life, and appear to fit an active-but-odd style described by Lorna Wing which is consistent with the clinical impressions of AD. Alternatively, ASD children predisposed to Behavioral Inhibition may be more inhibited in interactions, passive and less effective in early language learning, withdrawn and easier to identify earlier in life, and appear to better fit the aloof prototype of Autism.

Objectives: To examine this hypothesis, the influence of BAS/BIS on the behavior of higher functioning 8 to 16 year-olds with ASD was assessed using anterior EEG asymmetry measures. Left Frontal Asymmetry (LFA) is associated with BAS and Right Frontal Asymmetry (RFA) is associated with BIS. LFA- versus RFA-ASD children were expected to display significant differences on parent-report measures of global social communication impairment and indicators of pragmatic language. Children with LFA-HFA were also predicted to have later observed symptom onset than children with RFA.

Methods: EEG data were collected from 18 scalp sites for fifty-one ASD children. EEG asymmetry was computed for homologous frontal electrode pairs (e.g., lnF4-lnF3). Positive scores were

indicative of relative LFA. Data on social communication impairment and symptom onset were collected via parent report on the Children's Communication Checklist-Second Edition (CCC-2), and parent interview using the Autism Diagnostic Interview-Revised (ADI-R).

Results: Results indicated that parents of HFA children with LFA reported higher levels of general communicative competence on the CCC-2, GCC, F (3, 47) = 6.83, p = .01, but greater impairment on the CCC-2 scales of pragmatic communication when compared to RFA-HFA children, SIDC, F (3, 47) = 4.41, p < .05. Prior data suggests that this CCC-2 profile is common to AD. Additional analyses indicated parents reported that the anterior asymmetry subgroups displayed different developmental courses of symptom onset on the ADI-R ("Age When Abnormality First Evident") such that RFA was associated with early and more confident recognition of atypical (and stereotypically autistic) development, while LFA was associated with early, but less unambiguously autistic impairment, X^2 (51) = 3.75, p = .05.

Conclusions: This study demonstrates that anterior asymmetry subgroups are useful markers of phenotypic variability that may be meaningfully related to the course and expression of core symptoms of Autism. In particular, this study suggests that variability in measures of motivational predispositions to approach vs. avoidance behavior are associated with differences in early course and qualitative differences in communication impairment that have previously been associated with HFA versus AD diagnostic subgroups.

105.44 44 Spontaneous BOLD Signal Fluctuation in Resting State Functional MRI Demonstrates Difference in Hurst Exponent Distribution in Adults with and without Autism Spectrum Conditions.

M. C. Lai*[1], J. Suckling[2], B. Chakrabarti[3], M. V. Lombardo[3], E. Bullmore[2], S. A. Sadek[1], G. Pasco[1], S. J. Wheelwright[4], S. Baron-Cohen[4] and M. R. C. AIMS Consortium[5], (1)*Autism Research Centre, Department of Psychiatry, University of Cambridge*, (2)*Brain Mapping Unit, Department of Psychiatry, University of Cambridge*, (3)*University of Cambridge, Autism Research Centre*, (4)*University of Cambridge*, (5)*University of Cambridge; Institute of Psychiatry, King's College London; University of Oxford*

Background: Functional magnetic resonance imaging (fMRI) time-series are typically complex with variable local autocorrelation. After adequate motion correction, resting state fMRI signals can be modeled as fractional Gaussian noise (Maxim et al., 2005) described by two parameters: the Hurst exponent (H) and the signal variance. The Hurst exponent relates to the fractal dimension and describes the self-similarity of signals. Typically for fMRI time-series the range lies in 0.5<H<1, thus signals are positively autocorrelated and have so-called long-memory (persistent) behaviors. The spatial distribution of H in resting state fMRI corresponds to anatomical structures with significant differences between grey and white matter (Wink et al., 2008). Differences between patterns of H in neuropsychiatric conditions compared to neurotypical controls have been explored in Alzheimer's disease (Maxim et al., 2005) and attention-deficit/hyperactivity disorder (Anderson et al., 2006). Since long-memory processes measured by Hurst exponent could be related to long-memory oscillations from spontaneous neuron firing, and since autism spectrum conditions (ASC) may be underpinned by atypical neuron synchrony and connectivity, we predict differences in H in a cross-sectional study of adults with ASC compared to matched neurotypical controls.

Objectives: To assess the differences in the distribution of the Hurst exponent in spontaneous BOLD signal fluctuations from fMRI brain imaging in adults with ASC and matched controls.

Methods: 31 adult, right-handed males (18-45 years old) with a clinical and ADI-R confirmed diagnosis of ASC, and 33 age-, sex-, handedness- and IQ-matched neurotypical adults were scanned in a 3T MRI scanner by echo planar imaging in an eye-closed, awake, non-task resting state. Following preprocessing of the acquired images to correct for motion, maps of H were generated at each intra-cerebral voxel for each participant. These were then co-registered into the standard anatomical space of the Montreal Neurological Institute by affine transform and cross-section statistical analysis at the cluster level performed using permutation inference (CamBA v2.2.0 http://www-bmu.psychiatry.cam.ac.uk/software/).

Results: Statistical significance was set such one false positive cluster was expected under the null-hypothesis (equivalent p=0.003). At this level widespread increases in H were observed in

participants with ASC relative to controls, particularly in the limbic systems and the anterior cingulate.

Conclusions: These data provide preliminary evidence that H may be substantively different in resting neural oscillations in ASC compared with matched controls. The regions identified have previously been implicated with ASC using other imaging techniques and it seems therefore plausible that changes in the persistence of fMRI time-series reflect changes in the underlying neural systems associated with the condition.

105.45 45 Diminished Selectivity of the Social Brain in Individuals with Autism. N. B. Pitskel*[1], C. M. Hudac[2], S. D. Lantz[1], N. J. Minshew[1] and K. A. Pelphrey[2], (1)*University of Pittsburgh School of Medicine*, (2)*Yale University*

Background: Abnormalities in social behavior are pathognomonic of autism spectrum disorders. Considerable evidence has accumulated documenting abnormalities in face perception in ASD. Illustrating the nature of these deficits, individuals with autism exhibit abnormal visual scanpaths of faces as well as abnormal patterns of neural activation in several brain regions implicated in social cognition, including the fusiform gyrus (FFG), a region of the brain specialized for face processing, the superior temporal sulcus (STS), an area known to be involved in the processing of biological motion, and the amygdala (AMY), a region widely implicated in assessing the emotional significance of stimuli.

Objectives: We sought to characterize the neural substrates of abnormal gaze fixation in autism utilizing functional magnetic resonance imaging (fMRI). Specifically, we asked how brain regions involved in social cognition would differ in subjects with autism versus IQ-matched typically developing comparison subjects in response to dynamic social stimuli of somewhat greater ecological validity than commonly used still pictures of faces, by presenting a common and relatively simple social scenario.

Methods: Six subjects with autism (mean age 25.7 years, 5 males) and 4 typical controls (mean age 33.7 years, 4 males) underwent high-resolution fMRI in a 3-T scanner while viewing 6-sec computer-generated virtual-reality movies of a man approaching down a hallway (Run 1). In a second condition, the same videos were shown with a fixation cross-hair moving over the eyes of the figure; subjects were instructed to maintain fixation on the cross-hairs (Run 2). Subjects viewed 20 trials of each condition. Functional regions of interest (ROIs) were drawn in the FFG, STS, and AMY based on average activation of all subjects across both conditions. The ROIs were then applied to each group and condition separately, and hemodynamic responses were extracted for each region.

Results: The task resulted in significant activation across subjects in the right STS, bilateral FFG, and bilateral AMY. Examination of the hemodynamic response revealed an effect of group on latency in the right STS and bilateral FFG, with the onset of the BOLD response premature in autism as compared to controls for both conditions. Additionally, activation in the right FFG was greater for subjects with autism than for controls.

Conclusions: The FFG is known to be selectively activated by faces in typical individuals. The latency effect suggests that, rather than a selective response to the face that is stronger towards the end of the trial, when the virtual actor is closer to the subject and occupying more of the visual field, subjects with autism display a broadly responsive activation that peaks earlier, indicative of a lack of selectivity to the face stimuli. The earlier onset of activation in turn drives an overall greater magnitude at peak in subjects with autism as compared to neurotypical subjects. Similarly, the STS may be less specifically responsive to socially-relevant motion in autism, responding more broadly to motion in general. These findings implicate a relative lack of specialization of brain regions involved in social cognition in individuals with autism.

105.46 46 Neural Bases of Self Representation in High-Functioning Autism. C. L. Klein*[1], B. G. Travers[1], L. G. Klinger[1], M. R. Klinger[1] and R. K. Kana[2], (1)*University of Alabama*, (2)*University of Alabama at Birmingham*

Background: Previous research has indicated that impairments in self understanding in persons with Autism Spectrum Disorders (ASD) may contribute to difficulties in joint attention, social learning, and social cognition. Self-referential processing entails the ability to process information by incorporating self awareness and self memory. In neurotypical individuals, self-referential processing has been linked to several brain areas, including the dorsal medial prefrontal gyrus, left

inferior frontal gyrus, anterior and posterior cingulate cortices, and precuneus. Individuals with ASD have been found to show atypical activation pattern in some of these areas (Craik et al., 1999). In addition, activation in these regions has been correlated with difficulties in social communication and social cognition in persons with ASD (Ohnishi, 2000).

Objectives: The primary objective of this study was to measure the neural substrates underlying self representation in persons with ASD. This study also examined whether self-referential processing leads to enhanced memory in ASD, as it does in neurotypical individuals.

Methods: Eight high-functioning adolescents and adults with ASD and twelve age and IQ matched neurotypical individuals participated in this fMRI study (data collection is ongoing). Participants completed three judgment tasks with a button response of "yes" or "no": 1) the 'self' block in which participants judged whether the adjective described the participant, 2) the 'other' block in which participants judged whether the adjective described their favorite teacher, and 3) the 'letter' block in which participants judged whether the adjective contained the letter "e". Stimuli were positive and negative adjectives. The three judgment tasks were completed in a blocked design format with three blocks for each type of judgment. The fMRI data were acquired from a Siemens 3T Allegra scanner and analyzed using SPM2 software. After the scanning session, participants completed a recognition memory test consisting of 90 adjectives seen during the scan and 90 new adjectives. Additional measures were collected, including fluid reasoning, working memory, and symptomotology surveys and rating scales.

Results: No differences in participant responses to stimuli were found. Compared to controls, participants with ASD showed reliably less activation in several areas while processing self and other adjectives compared to performing letter identification. These include less activation in the medial prefrontal cortex, an area previously associated with social-cognition and self-referential thinking, and the left inferior frontal and left posterior superior temporal regions, areas associated with language processing. In ASD, there was no difference in the number of words recalled in "self" and "other" conditions during the memory test (in contrast to previous research in this area), while controls showed an advantage in memory for words in the self conditions.

Conclusions: These findings suggest less socially and semantically oriented processing of information related to self and others in persons with ASD. They also underscore the important role the medial prefrontal cortex plays in social cognition and self-referential thinking. Moreover, the behavioral (memory) and neuroimaging (hypoactivation of the medial prefrontal cortex) results suggest that self-referential processing may not have a privileged neural status in persons with autism.

105.47 47 Neural Activity in Mirror Neuron and Reward Circuitry While Viewing Emotional Expressions Relates to Core Deficits in Autism. J. D. Rudie*, A. Martin, L. A. Borofsky, A. A. Scott, S. Bookheimer, M. Iacoboni and M. Dapretto, *University of California, Los Angeles*

Background: The social deficits observed in autism spectrum disorders (ASD) have been linked to dysfunction in the mirror neuron system (MNS; see Oberman & Ramachandran, 2007, for review). For instance, we previously showed that high-functioning children with ASD showed less MNS activity than typically-developing controls while observing emotional expressions, and that the level of mirror-related activity seen in children with ASD was negatively related to symptom severity in the social domain (as measured by both ADI-R and ADOS-G; Dapretto et al., 2006). According to the social motivation hypothesis of autism, social stimuli such as faces may not be attended to by individuals with autism as they may not find them 'rewarding.' Surprisingly, activity in reward-related circuits in response to social stimuli has been largely unexplored in individuals with autism (Scott at al., under review).

Objectives: In this study, we used fMRI to further characterize the relationship between core autism deficits and activity in both MNS and reward circuitry. We used parental reports on the Social Responsiveness Scale (SRS), a validated measure of clinically significant autism traits, and examined how scores on this scale would relate to neural activity in a priori regions of interest including MNS (right IFG), limbic (amygdala, insula), and reward-related areas (ventral striatum) as well as other 'social brain' regions (e.g., medial prefrontal cortex).

Methods: Twenty high-functioning children with

autism (19 males; mean age: 12.35) completed an fMRI task involving passive observation of faces displaying different emotions (angry, fearful, happy, sad, and neutral). Using an event-related design, each face was presented for two seconds according to an optimized random sequence, which included null events (fixation crosses) and temporal jittering. Multiple regression analyses (controlling for the effects of IQ) were conducted to relate neural activity during this task to SRS total scores, as well as scores on the SRS treatment subscales (Social Motivation, Social Communication, Social Cognition, Social Awareness, and Autistic Mannerisms).

Results: Analyses revealed significant negative correlations between the SRS total score and activity in the right IFG, insula, and amygdala, as well as in the ventral striatum and medial prefrontal/anterior cingular cortex. Separate regressions with the treatment subscales of the SRS showed a similar pattern of results with the strongest correlations observed for the Social Motivation subscale. Somewhat surprisingly, the Autistic Mannerisms subscale also showed strong correlations within these networks, followed by weaker correlations with the Social Communication and Social Cognition subscales. Interestingly, no significant correlations were observed for the Social Awareness subscale which taps sensory aspects of reciprocal social behaviors.

Conclusions: These findings provide further evidence of a relationship between deficits in the MNS and severity of autism symptomatology, including aspects that have not been previously tied to MNS dysfunction such as restricted interest and stereotypical behaviors. Furthermore, the strong correlations observed between scores on the Social Motivation subscale and activity in both MNS and reward circuitry lend support to the social motivation hypothesis of autism and suggest that the social motivation deficits characteristics of autism might be related to MNS dysfunction.

105.48 48 Magnetic Resonance Spectroscopy in ASD: Review of Regions Investigated, Findings, Potential Influence of Methodology, and Directions for Future Research. N. Shetty[1], E. Ratai[1], A. P. Ringer[2] and M. Herbert*[1], (1)*Massachusetts General Hospital*, (2)*University of California, Berkeley*

Background: Growing documentation of metabolic alterations in autism increases the need to characterize metabolism in brain tissue. Magnetic Resonance Spectroscopy (MRS) is constrained by the impossibility of performing whole brain acquisitions and the need to place localized voxels, as well as the impact of acquisition protocols on findings. Literature review can contribute to well-targeted choice of future research design.

Objectives: To consider the potentiality of MRS for measuring metabolites pertinent to emerging metabolic findings in ASD and from this vantage point to produce a systematic and critical overview of MRS investigations in ASD to date.

Methods: PubMed was searched for papers on MRS in ASD as well as brain metabolites. Relevant papers were reviewed and tabulated based upon regions of interest, absolute metabolite concentrations and/or ratios in each region studied, field strength, repetition time (TR) and time to echo (TE), subject characteristics (age, gender, diagnosis, use of sedation) and objectives (e.g. neurocognitive, pathophysiological or developmental).

Results: Regions chosen for investigation were scattered with many visited in only one study. For some regions studied multiple times the literature contains contradictory findings, possibly attributable to different acquisition protocols and/or subject and cohort heterogeneity.

Conclusions: The application of MRS is strongly hypothesis dependent given the need to place localized voxels, and also the impact of acquisition protocols on findings. Some of the most critical metabolites to measure from a metabolic standpoint (e.g. GABA, glutamate, glutathione, energy and membrane phosphates and phospholipids) as well as critical methods of acquisition (e.g. 31P, spectral editing techniques) have been underexplored, in part due to significant technical challenges. We hope that this systematic review will contribute to more effective and coordinated targeting of future investigations.

105.49 49 Failure of Right Hemispheric Suppression Underlies Bilaterality. T. J. Druzgal*[1], J. S. Anderson[1], A. Froehlich[1], N. Lange[2], M. DuBray[1], E. Bigler[3], M. P. Froimowitz[2] and J. E. Lainhart[1], (1)*University of Utah*, (2)*Harvard University*, (3)*Brigham Young University*

Background: Individuals with autism spectrum disorders often exhibit atypical language patterns including delay of speech onset, literal speech interpretation, and poor recognition of social and emotional cues in speech. Previous studies have noted tendency towards left-handedness in autistic populations with increased right hemispheric processing of language in autism. We examined stability of language lateralization during the course of a language stimulus using

fMRI in control and high-functioning autistic populations.
Objectives: Determine whether increased right hemispheric processing of language results from increased right hemispheric activity or decreased left hemispheric activity relative to controls.
Methods: Twenty-five right-handed subjects (13 high-functioning autistic, 12 control) were studied using auditory and visual sentence completion tasks, and areas of differential activation between groups were identified. Hand preference was measured by Edinburgh Handedness Inventory and included as a covariable in the analysis.
Results: Autistic subjects showed significantly increased activation of right Wernicke's area compared to control subjects. After adjustment to account for differences in hand preference among groups, this difference persisted. Time series traces showed that both populations initially activated both hemispheres during the course of a language stimulus, but control population showed suppression of right-hemispheric activation as the stimulus progressed while autistic population did not.
Conclusions: Both autistic and control populations showed bilaterality of language processing in initial phases of language activation. As language stimulus progressed, autistic subjects did not show suppression of right-sided activation. This may represent a mechanism for language disturbances in autism in which extraneous information is not appropriately suppressed.
The project described was supported, in part, by Grant Number RO1 MH080826 from the National Institute Of Mental Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute Of Mental Health or the National Institutes of Health.

105.50 50 Anterior Cingulate Connectivity in Children with Autism Spectrum Disorders. A. Di Martino*[1], A. M. C. Kelly[1], D. G. Gee[1], Z. Shehzad[1], M. Mairena[1], R. Grzadzinski[1], L. Q. Uddin[2], P. T. Reiss[3], E. Petkova[3], C. Lord[4], F. X. Castellanos[1] and M. P. Milham[1], (1)*Institute for Pediatric Neuroscience*, (2)*Stanford University*, (3)*NYU Child Study Center*, (4)*University of Michigan*

Background: Converging lines of evidence support models of autism spectrum disorders (ASD) as developmental dysconnection syndromes, characterized by increased short-range connectivity and reduced long-range connectivity in the brain. Initially based on findings of white matter abnormalities during development, such models have gained support from recent evidence of autism-related decreases in cortico-cortical functional connectivity (FC) in task-based studies. Two initial studies, using recently emerging resting state fMRI approaches to map FC, have shown FC abnormalities between the pregenual anterior cingulate cortex (pgACC) and medial prefrontal cortex in adults with ASD. However, to date no resting state fMRI research has been conducted in children with ASD.

Objectives: As a first step to characterize the pattern of FC in youth with ASD, we examined FC of the pgACC network in school-age children with ASD. The pgACC network was chosen based on both its role in social cognition and its consistent pattern of ASD-related hypoactivation in social processes.

Methods: Seven children with ASD (10.8 y ± 1.7; 3 girls; 6 with Autism and 1 with PDD-NOS) and seven age- and sex-matched NC completed a 6.5 min resting state fMRI scan (field strength= 3 T; TR = 2000 ms; voxel 3x3x3mm). All children and their parents signed an NYU IRB approved assent and consent form, respectively. Preprocessing included slice-time correction, motion correction, bandpass temporal filtering, spatial filtering, and spatial normalization. A spherical region of interest centered in the pgACC was selected as the seed region for FC analyses. For each participant, FC analyses were carried out using multiple regression (implemented in FSL's FEAT) including the timeseries of the pgACC seed, and nine nuisance covariates as predictors (i.e., movement, white matter, global signal, and CSF). Group analyses using random effect models implemented in FLAME were carried out. Corrections for multiple comparisons were performed at the cluster level using Gaussian random field theory (min $Z > 2.3$; cluster significance: $p \leq 0.05$, corrected). Further, we computed the number of short- and long range connections by measuring the Euclidean distance (cutoff=45 mm) between the center of the seed ROI and every other voxel that reached significance in the group-level thresholded Z-score maps.

Results: Children with ASD demonstrated higher degrees of local connectivity in the pgACC network. This pattern was quantitatively evident as an increased number of significant voxels connected within 45 mm Euclidean distance from the pgACC. Consistent with their young age,

neither group showed a high degree of significant long-range FC between pgACC and the posterior component of the network (posterior cingulate cortex).

Conclusions: Our preliminary findings suggest that ASD are characterized by greater short-range connectivity in the pgACC network. Data collection is still ongoing to reach a sample size of 20 children per group. Attainment of our aims would further implicate the social-processing pgACC network in autism, as well as motivate translational studies on the neuronal developmental processes that drive increases in short-range connectivity and decreases in long-range connectivity.

105.51 51 Impaired Prefrontal Cortical Response by Switching Stimuli in Autism Spectrum Disorders Assessed by near-Infrared Spectroscopy. A. Saotome*[1], M. Tazoe[2], M. Narita[3], K. Sakatani[4] and N. Narita[1], (1)*Bunkyo University*, (2)*Japan Lutheran College*, (3)*Mie University*, (4)*Nihon University School of Medicine*

Background: Impairments in various kinds and degrees of higher-order cognitive processing related to prefrontal cortex (PFC) are reported in autism spectrum disorder (ASD) patients. We have previously reported the lack or delayed oxygenation of prefrontal cortex (PFC) when task-switch paradigm was conducted to ASD subjects using near-infrared spectroscopy (NIRS), suggesting a failure in timely switching of signal processing in the PFC upon stimulation in ASD (IMFAR 2008).

Objectives: We aim to further investigate the reactive pattern of PFC in ASD upon consecutive exhibit of cognitive and less-cognitive stimulation, by using geometrical figure-memorization paradigm in which working memory requiring task (WM) and non-working memory requiring task (NWM) are alternately appeared.PFC oxygenation level was measured by NIRS during the paradigm.

Methods: Preliminary 11 ASD subjects (IQ>65 by WISC III, ages of 14-46, mean 29.5 y.o., 3 males and 8 females) and 14 healthy controls (ages of 19-51, mean 27.3 y.o, 1 male and 13 females) were studied. The task-switching paradigm was designed using randomized geometrical figures in combination of three shapes (circle, triangle, and square) and four colors (red, yellow, blue, and green). For WM, subjects were required to memorize figures which appear one by one every 3 seconds on a PC screen, and subsequently were ordered to touch the figures in consecutive order as they memorized, from a multiple choices appeared on the screen. For NWM, all test figures are already appeared with the multiple choices so that the subjects can touch the figures while watching them. The number of figures was gradually increased up to 6.
PFC oxygenation was continuously measured by NIRS during the task performance, and the oxygenated Hb level in PFC during each task was examined between control and ASD subjects.

Results: The NIRS parameters during each task were normalized and averaged. In the controls, oxygenated Hb level was increased during WM and decreased during NWM, and was gradually elevated when the number of figures is increased, suggesting that in the control PFC, shifting of signal processing was sensitively occurred according to the task switch. Additionally, laterality of right PFC was consistently observed in the controls, which is predictable from the nature of the present paradigm that requires spatial cognition.
On the contrary, ASD subjects lack the clear switching tendency of PFC oxygenation according to the WM/NWM switch, and obvious right PFC laterality was not observed. However, the task performance of ASDs was not necessarily worse than the controls. The comparison of oxy-Hb transition curve during the whole tasks were significantly different between controls and ASDs (Rt $p<0.001$, Lt $p<0.05$, controls vs ASDs respectively by two-way ANOVA)

Conclusions: Our present study revealed that a rapid and obvious response of PFC oxygenation to the incoming switching stimuli was not observed in ASD subjects, which may explain their difficulties in the daily life, the school, or work. Several ASD subjects showed rather superior performance rate in harder task, which might be an important clue to understand their superiority in particular brain functions.

105.52 52 Resting State EEG Connectivity in Children with HFA. J. R. Wiersema*, R. Raymaekers and H. Roeyers, *Ghent University*

Background: There is a growing body of evidence indicating that autism is a biologically based disorder, related to atypical patterns of cortical connectivity. As distributed brain networks underlie higher cognitive, socio-emotional, and

communication functions, impaired functional connectivity could relate to clinical manifestations of autism. Functional cortical connectivity can, in a non-invasive way, be studied by means of EEG coherence.

Objectives: To investigate functional cortical connectivity in children with high-functioning autism (HFA) during resting state, by means of EEG coherence.

Methods: Normally intelligent children (9 to 13 years) with HFA were compared with age-matched normally developing peers. Eyes-closed resting EEG was measured for three minutes, using a 128-channel EEG system. Inter- and intra-hemispheric coherence measures were calculated for delta, theta, alpha, and beta frequency bands.

Results: No main group differences were found for inter-hemispheric coherence measures. However, a significant group by hemisphere effect was found for slow wave EEG (delta and theta) coherence. This effect was caused by the combination of enhanced connectivity in the left hemisphere and reduced connectivity in the right hemisphere for the HFA group, indicating atypical lateralisation.

Conclusions: Differences in resting state EEG connectivity were noted between groups, suggestive of abnormal functional brain lateralisation in autism. The findings support the disturbed cortical connectivity model of autism.

Sponsor: Ghent University Research Fund

105.53 53 The Mirror Neuron System as Evidenced by Attenuation of EEG Mu Rhythm and Social Aptitude in Autism Spectrum Disorders. B. Aaronson* and R. Bernier, *University of Washington*

Background: The mirror neuron system (MNS) activates in response to observing and executing a motor action. Though originally observed via single neuron recording in monkeys (Rizzolatti et al., 1996), it is evidenced in humans through the attenuation of the mu rhythm observed via electroencephalography (EEG). This system is suggested to be the biological basis of imitation (Rizzolatti & Craighero, 2004). Some theories place imitation at the core of the developmental course of ASD (Rogers & Pennington, 1991), and MNS dysfunction has been demonstrated in ASD populations (Oberman et al., 2005, Bernier et al., 2007).

Objectives: To examine mu attenuation and its relationship to autism symptomology.

Methods: EEGs were collected during the observation of biological movement (simple grasping motion) from a sample of adults with an autism spectrum disorder (ASD, N=15) and typical development (TYP, N=14). Ratio of the power in the 8-13 Hz band recorded from 16 central electrodes at the C3 and C4 sites during observation relative to resting power was calculated and log transformed as a measure of mu attenuation. A caregiver report of autism symptomology on the Autism Spectrum Quotient (AQ) was collected and the relationship between mu attenuation and autism symptomology was calculated.

Results: Analysis reveals a significant correlation between mu attenuation and scores on the social skills subscale of the Autism-Spectrum Quotient (AQ) in the AUT group ($R2=.551$, $p<.03$), most pronounced in the left hemisphere ($R2=.592$, $p<.02$). No significant correlations were found between mu attenuation and other AQ subscales. Additionally, no significant correlations were observed in the TYP group.

Conclusions: Our results are consistent with recent findings extending the involvement of the MNS beyond motor-execution/observation to include social abilities. Other studies have implicated the MNS in the interpretation of context and intention (Iacaboni et al., 2005), as well as the interpretation of social stimuli (Oberman et al., 2007). Our findings further demonstrate a connection between the mirror neuron system and imitation and its consequence in social aptitude.

105.54 54 Functioning of the Mirror Neuron System in Children with HFA during Observation and Imitation of a Precision Grip: An EEG Study. R. Raymaekers*, J. R. Wiersema and H. Roeyers, *Ghent University*

Background: During passive observation of actions performed by others, cortical brain regions that are also involved in the execution of actions, become activated. These regions form an observation/execution matching system, the so-called mirror neuron system, which contributes to action comprehension and imitation by translating visual input into motor understanding. Previous research has suggested that a dysfunction of this system may underlie the characteristics of autism, such as deficits in imitation, theory of mind,

empathy and pragmatic language. In addition, studies have shown that the reduced power of the mu frequency EEG oscillations (8-13 Hz) during action performance and observation of human movement indicates MNS activity.
Objectives: To investigate the MNS activity in children with high-functioning autism (HFA) during imitation, execution, and observation of a goal/object-oriented movement.

Methods: Normally intelligent children (9 to 13 years) with HFA were compared with age-matched normally developing peers. The children were asked 1) to observe a picture of a manipulandum, 2) to observe a precision grip of a manipulandum, 3) to observe a simple hand movement, 4) to imitate a precision grip and 5) to self-initiate the previous seen precision grip. During these conditions, 128-channel EEG was recorded.
Results: Preliminary results indicate that mu suppression is comparable between the HFA and the control group in action-imitation/execution conditions, as well as in action-observation conditions. Further analyses are currently in progress.

Conclusions: These preliminary findings give no support to the hypothesis of an impaired MNS in school-aged children with HFA.

105.55 55 ERP Responses to Faces Are Correlated with Verbal Skills in Toddlers with ASD. E. J. H. Jones*[1], S. J. Webb[1], K. Merkle[1], N. Freed[1], J. Greenson[1], M. Murias[1] and G. Dawson[2], (1)*University of Washington*, (2)*Autism Speaks, UNC Chapel Hill*

Background: Event-related potentials (ERPs) have previously indicated that face processing may be atypical in 3- to 4-year-old children with ASD (e.g. Dawson et al., 2002; Webb et al., 2006). However, little is known about the relationship between face processing and other skills early in the development of ASD. The present study examined neural responses to faces in 18 to 30-month-old toddlers with ASD in comparison to a group of age-matched typically developing toddlers (TD).
Objectives: To examine neural responses to familiar and unfamiliar faces in 18- to 30-month-old children with ASD and typically developing children, and their relation to age, IQ and adaptive skills.
Methods: In addition to developmental and diagnostic testing (including the Mullen Scales of Early Learning, the Vineland Adaptive Behavior scales, the ADOS and the ADI-R Toddler), toddlers viewed color photographs of their mother and a stranger in an ERP procedure. Brain activity was continuously recorded using a 128-electrode Geodesic Sensor Net (Electrical Geodesics, Inc.). Offline, artifact-free trials from each category were averaged together, re-referenced to an average reference, and baseline corrected. Children's data was only included in the final analyses if they had 10 or more artifact-free trials per condition. Data were averaged across time windows and electrode groups chosen with reference to the grand average waveform.
Results: Preliminary analyses suggest the Nc amplitude response to both face types was significantly more right lateralized in the ASD group than the TD group over anterior electrodes. Preliminary correlation analyses showed that a larger Nc correlated with older age in the TD group, but not the ASD group. In contrast, a larger Nc correlated with higher verbal ability in the ASD group, but not in the TD group.
Conclusions: Preliminary results suggest that the lateralization of event-related potential responses to facial stimuli may differ in toddlers with ASD. Further, neural responses to faces may not show the same developmental trajectory in toddlers with ASD as in typically developing toddlers. Finally, there may be a relation between verbal and communication skills, and neural responses to faces in toddlers with ASD. We are currently conducting analyses of data from a group of children with general developmental delays in order to explore whether these findings are specific to toddlers with ASD.

105.56 56 Multisensory Interactions Between Somatosensory Stimulation and Vision in Autism Spectrum Disorders: An Electrophysiological Study. N. Russo*[1], J. J. Foxe[2], M. Tommerdahl[3] and S. Molholm[1], (1)*The Children's Research Unit (CRU), Program in Cognitive Neuroscience,City College of New York*, (2)*City College of New York*, (3)*University of North Carolina*

Background: Simultaneously presented multisensory stimuli are automatically integrated by typically developing individuals (TD) and frequently lead to enhancements in the ability to make behavioral discriminations in relation to unisensory inputs. For example, simply looking at the body part where somatosensory stimulation is taking place appears to improve somatosensory discrimination (e.g., Taylor-Clarke & Haggard, 2002). This may result from the coordination of visual and somatosensory spatial maps, and indeed the multimodal nature of spatial attention would argue for just this outcome. Corresponding

electrophysiological measures reveal that the somatosensory response is increased in amplitude when the stimulated location is observed compared to when it is not, suggesting that a magnification or better titrated tuning of the cortical response contributes to improved behavioral performance. In Autism Spectrum Diagnoses (ASD) there is a hypothesized reduction in the integration of information across cortical areas and evidence for impaired multisensory processing. Since visual somatosensory integration requires long range connectivity, visual influences on somatosensory processing might be reduced in this population.

Objectives: To examine the influence of vision on somatosensory processing in children with ASD, using a task with known behavioral and electrophysiological signatures.

Methods: A cohort of high functioning adolescents with ASD and IQ, gender, and handedness matched typically developing (TD) adolescents will complete a forced choice intensity discrimination task to assay performance thresholds across four conditions: eyes closed (unisensory), view object (uninformative vision), view stimulated arm (informative vision), and view non-stimulated arm (vision directed at a different spatial location). Participants determine which of two stimulations presented simultaneously (in a staircase method) on the back of the left hand is more intense via a button press. Discrimination thresholds are acquired concurrently with ERPs.

Results: Preliminary analysis reveal significant interactions in behavioral discrimination thresholds between the informative vision and eyes closed conditions for the TD group, with better performance in the multisensory condition. We expect a different pattern of results for the adolescents with ASD with a) discrimination thresholds expected to be better for the ASD versus the TD group (e. g., Cascio et al., 2007; Tommerdahl et al., 2007) and b) less benefit in ASD from viewing the area where somatosensory stimulation is applied.

Conclusions: Individuals with ASD show enhanced discrimination abilities in relation to typically developing individuals across several modalities that includes touch (O'Riordan & Passetti, 2006; Tommerdahl, 2007) as well as instances of atypical multisensory integration (e.g. Bebko, et al., 2006; Russo et al., in prep; Smith & Bennetto, 2007). Together these findings suggest that behavioral and electrophysiological modulations of vision on somatosensation may differ in ASD. The findings from the present study will be discussed with respect to theories of multisensory integration and enhanced discrimination abilities, and will provide both behavioral and electrophysiological evidence regarding the integrity of multisensory systems and spatial tuning in children with ASD.

105.57 57 Crowding Effect in Autism Spectrum Disorders. P. A. Constable*[1], J. A. Solomon[1] and D. M. Bowler[2], (1)*City University*, (2)*City University, London*

Background: Visual processing of information by individuals with autism spectrum disorders (ASDs) is different to normally developing individuals. One aspect of the visual sense is the retinotopic representation of visual space within the visual cortex. How visual space is represented in the visual cortex is of interest because individuals with ASD display higher performance in visual search tasks. One factor that may affect performance on visual search tasks is crowding. In normal observers, identification of items in the visual periphery is impaired when other items are nearby. A reduced susceptibility to visual crowding may be the reason that individuals on the autism spectrum have been reported capable of outperforming normal observers in visual search for ellipses.
Objectives: To ascertain acuities for elliptical eccentricity and the critical spacings at which crowding impairs object identification.
Methods: Participants for this study were selected from a panel of volunteers that were matched for verbal, performance and full IQ. ASD participants met DSM-IV criteria confirmed by ADOS and review of clinical notes. Ethical approval was granted by University Ethics committee.
Preliminary data have been collected from 6 ASD participants and 2 matched control subjects. We anticipate a total of 15 observers from each group.
An iMAC 7.1 computer running MATLAB™ (MathWorks Ltd) was used for stimulus generation, experiment control and recording subjects' responses. The programs controlling the experiment incorporated elements of the PsychToolbox. Stimuli were displayed on an ATI Radeon HD 2600 Pro monitor (1680 x 1050 pixels), driven by the computer's built-in graphics card. The observer was seated at 70 cm from the

screen using their habitual optical correction if required. A central white spot 3 x 3 pixels was used for fixation. Short (120 ms) presentations guaranteed that our observers were unable to initiate an eye movement prior to the disappearance of our elliptical targets, which appeared at E = 3.9 deg, randomly to the left or the right of the fixation spot.
In the first phase of the experiment an adaptive staircase was used to converge on the 'threshold' elliptical eccentricity required for observers to discriminate between vertical and horizontal ellipses with 81% accuracy. In the second phase two circles flanked the target on its left and right. Each target's elliptical eccentricity was fixed at √2 times the observer's threshold. An adaptive staircase converged on the 'critical' target-flanker distance with which the target's orientation could once again be identified with 81% accuracy.
Results: All results are expressed as mean ± sd. Acuity (1/threshold) was 3.50 ± 0.98 for the ASD group and 4.81 ± 1.38 for the matched participant group. The difference between groups was not significant (unpaired, two-tailed T-test: p=0.06). Critical spacing was 0.58E ± 0.11E for the ASD group and 0.62E ± 0.17E for the matched participants. Again, the difference was not significant (p=0.66).
Conclusions: These preliminary findings indicate that there are no differences in acuity or the effects of crowding between individuals with ASD and the comparison group.

105.58 58 Electrophysiological Correlates of Audio-Visual Integration of Spoken Words in Typical Development and Autism Spectrum Disorder. O. Megnin*[1], A. Flitton[1], M. De Haan[1], C. R. G. Jones[2], T. Baldeweg[1] and T. Charman[2], (1)*UCL Institute of Child Health*, (2)*Institute of Education, University of London*

Background: In a previous electrophysiological (ERP) study examining audio-visual (AV) integration of speech in typically developing adults we found a speeding up and attenuation of the auditory N1 component specific to an AV condition with informative or predictive lip movements. This N1 attenuation correlated with an earlier increased fronto-polar negativity (FPN) raising the possibility of a top-down modulation effect. The present study examines ERP correlates of AV integration of spoken words in typically developing (TD) adolescents and adolescents with autism spectrum disorder (ASD). There are a number of reasons why we might expect to see differences in an autistic population, including atypical unimodal auditory processing (e.g. Bomba & Pang, 2004), atypical unimodal visual processing, particularly with regards to face processing (e.g. McPartland et al, 2004), and multi-sensory processing differences (e.g. Bebko et al, 2006; Magnee et al, 2008).

Objectives: The present study will examine whether the adult pattern of AV integration effects are replicated in a group of TD adolescents and whether the ERP correlates of multisensory integration are different in adolescents with ASD compared to TD adolescents.

Methods: ERPs were recorded from 19 TD adolescents and 14 adolescents with ASD while they were presented with monosyllabic words in one of five conditions: audio-only (A), visual-only (V), audio-visual with face (AVF), audio-visual with scrambled face (AVS), and visual-only scrambled face (VS). Significant multisensory interactions [AVF - (A+V)] > 0 were examined.

Results: Preliminary results suggest that in both autism and typical development, only approximately half of participants show the adult pattern of AV integration. Amongst those showing the FPN and N1 attenuation effects there are differences between the autistic and typically developing adolescents. Namely, TD adolescents show AV integration effects in the P50 but adolescents with ASD do not, the amplitude of the FPN effect was greater in the TD group than the ASD group, and the N1 attenuation and FPN effects were correlated in the TD adolescents but not the ASD adolescents. Spectral analysis of the EEG is currently being conducted to attempt to elucidate differences between subgroups (both TD and ASD) and differences between TD and ASD adolescents.

Conclusions: The electrophysiological correlates of AV integration appear to undergo a developmental maturation well into young adulthood, in both TD and ASD individuals. ERP correlates also imply that the AV integration process is different in ASD.

105.59 59 ERP Responses to Probe Words Following a Sentence Context during Reading in Individuals with Autism Spectrum Disorders: An MEG Study. B. Ahtam*, S. Braeutigam and A. Bailey, *University of Oxford*

Background: Numerous studies have shown that individuals with ASD have difficulties in spontaneous use of sentence context during reading.

Objectives: To use magnetoencephalography (MEG) to study the neural basis of abnormalities in sentence context effects in individuals with ASD.

Methods: 22 individuals with ASD and 22 typically developing (TD) adults participated in the study. Participants were matched on age, gender, and IQ. All measurements were taken at the Oxford Neurodevelopmental Magnetoencephalography Centre using a Neuromag-306 VectorView™ system, providing a helmet-shaped array of 102 pairs of gradiometers. Participants read sentences ending either with a homonym (dominant vs. subordinate meanings) or an unambiguous word. The sentences were followed by a probe word that was semantically related or unrelated to the meaning of the sentence. Participants were asked to indicate whether the probe word was related or unrelated to the meaning of the sentence that it followed and to give their responses with a key press. This study has been approved by the local NHS (UK) Ethics Committee. All participants gave written informed consent before the experiment.

Results: At 100ms both TD and ASD groups show similar activity for all the probe word conditions except for the DHR (related probe word that follows a dominant homonym final word) condition in the ASD group which shows a stronger response over the occipital and posterior-parietal areas. The word response at 150ms is stronger over the left temporal areas in the TD group than in the ASD group, in all probe word conditions. Between 200-300ms both groups show bilateral activity over the temporal and occipital areas. At N4-like latencies, both TD and ASD groups show stronger responses to the unrelated probe words, with stronger activity observed over right temporo-parietal areas for the unrelated conditions in the ASD group.

Conclusions: These results suggest that the ASD group exhibit close to typical patterns for the evaluation of semantic relatedness at the 450ms latency. The initial stages of the probe word activity in ASD shows dissimilarities from the TD group, which may indicate the existence of different processing strategies.

105.60 60 Filling-in in Autism: a High-Density Electrical Mapping Study of Visual Object Binding Mechanisms. T. S. Altschuler*[1], S. Molholm[1], D. Blanco[2], A. C. Snyder[1], A. B. Brandwein[1], N. Russo[1] and J. J. Foxe[2], (1)*The Children's Research Unit (CRU), Program in Cognitive Neuroscience,City College of New York*, (2)*City College of New York*

Background:

As well as the obvious clinical behavioral manifestations of Autism, it is now apparent that differences in very basic sensory-perceptual processing of environmental inputs may also be a core feature of Autistic Spectrum Disorder (ASD). For instance, early visual processing of object boundaries in late teens and young adults with ASD appears to be atypical (Vandenbroucke et al., 2008). In viewing occluded or partially fragmented objects, a typical adult brain can readily "fill-in" the missing information. That is, the brain is capable of binding disparate "local" elements into unified "global" wholes. One excellent means of studying this "filling-in" phenomenon involves the use of so-called illusory contour (IC) stimuli. Pacman-shaped disks are oriented with their "mouths" open and pointed towards each other such that they induce the perception of the contours of an illusory shape, even though no such contours physically exist. Event-related potential studies (e.g. Murray et al., 2002, Foxe et al., 2005) have extensively investigated this phenomenon and established a set of robust dependent measures that represent binding processes within the ventral visual stream. In particular, an early automatic contour-definition ERP component occurs between about 110-180 ms, and this has been termed the *IC effect*.

Objectives:

To investigate object-binding processes in persons on the autistic spectrum, using a well-established metric of ventral visual stream processing, the *IC effect*. In particular, we manipulated the spatial disparity of the Pacman inducers on the premise that binding across greater spatial scales might be progressively more dysfunctional in ASD.

Methods:

ERPs to IC stimuli were compared between typical and ASD children, aged 7-15, and also in a normal healthy adult cohort. IC inducing stimuli were presented at three progressively greater retinal eccentricities (4, 7 and 10 degrees respectively). The IC effect was measured for each eccentricity. Behavioral measures of global/local processing styles (Children's Embedded Figures Test (Witkin et al, 1971)) were also analyzed to assess any

contributions these differences might make to group differences.

Results:

Preliminary results from typical adults replicate Murray et al's (2002) *IC effect*, and show that this effect is evident at all three eccentricities. This pattern was replicated in typically developing children. Preliminary data from ASD children, however, suggest a less robust IC effect, even for the smallest degree of retinal eccentricity.

Conclusions:

If this pattern of results holds as our sample of ASD and TD children increases, it would point to a basic deficit in automatic object-binding mechanisms in ASD. The interaction between retinal eccentricity of the stimuli and diagnosis could begin to reveal specific ways in which automatic processes of people on the spectrum are like and unlike their typical counterparts.

105.61 61 The ERP Old-New Word Repetition Effect in Autism Spectrum Disorder: Abnormal Neural Functioning Underlying Typical Recognition Memory Performance. E. Massand*[1], D. M. Bowler[1], L. Mottron[2], A. Hosein[3] and B. Jemel[4], (1)*City University, London*, (2)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (3)*Hopital Rivière des Prairies*, (4)*Research, Lab, Neurosciences, and, Cognitive, Electrophysiology*

Background:

Although recognition memory in ASD (Autism Spectrum Disorder) tends to be undiminished compared to typically developing individuals (Bowler et al., 2000), it is still unknown whether memory processes in ASD rely on similar or qualitatively different mechanisms than those underlying recognition memory in typical development. One way to investigate this is to record online brain electrical activity during item recognition at test in ASD individuals and age- and IQ-matched typically developing individuals. Previous event-related potential (ERP) studies have shown that recognition of previously studied words is indexed by enhanced positive potentials of words that are correctly identified as 'old' from an earlier study phase, compared to words correctly identified as 'new' (known as old-new ERP effect). This effect is argued to reflect cognitive strategies engaged during recognition of an item and the recall of its contextual information.

Objectives:

The objective of the study was to investigate the ERP old-new recognition effect in adults with autism spectrum disorder.

Methods:

Data are currently available for 8 adults with ASD (mean age of 25.5 years and mean VIQ of 101) and 6 typical adults (mean age of 25.4 years and mean VIQ of 99). Expected group sizes are 15 participants in each group. Participants engaged in a yes/no recognition task, in which they studied 6 blocks of 50 words. After each block they were tested on the 50 study words and 25 lures. Study and test words comprised 450 French nouns (300 targets and 150 lures) extracted from the Baudot (1992) French dictionary. Matching was done on frequency, imagability rating and number of syllables. Starting letters were equated for every 1 in 4 words between target and lure. ERPs were collected from 64 scalp sites and averaged according to correctly recognized old words and correctly rejected new words.

Results:

Behavioural data revealed no overall differences in recognition between the ASD group and comparison group (corrected hit-rate proportions of 0.54 and 0.60 and standard deviations of 0.19 and 0.27 respectively. F (1, 12) = 0.124). ERP data revealed diminished Old-New ERP effects in the ASD group when compared to the typically developing group, mainly at the central and fronto-central scalp sites. In addition, the old-new effects were shorter-lasting in ASD than in typical participants. Indeed, the onset of the old-new ERP differences was approximately 300ms for both groups, ending approximately 700ms in the ASD group and lasting well on into 1700ms for the comparison group.

Conclusions:

The enhanced ERP positivity for old words in typical individuals is assumed to reflect the

engagement of cognitive strategies to aid the recognition of an old word (Cycowicz et al., 2001). The short lasting and diminished old-new ERP effect in ASD found here, indicates that ASD individuals do not utilise cognitive strategies in a similar manner to typically developing individuals. This study is the first to demonstrate abnormal old-new ERP repetition effects in ASD.

105.62 62 Increased Eye-Blink Rate in Autism Spectrum Disorder May Reflect Dopaminergic Abnormalities. B. Jensen[1], B. Keehn[2], L. Brenner[3], S. P. Marshall[1], A. J. Lincoln[4] and R. A. Müller*[1], (1)*San Diego State University*, (2)*San Diego State University / University of California, San Diego*, (3)*University of California, Los Angeles*, (4)*Alliant International University*

Background: Elevated blink rates have been related to overactivity of the central dopaminergic systems (Karson, 1983). In the only existing study of eye-blinks in autism spectrum disorder (ASD), Goldberg et al. (1987) found elevated blink rates in low-functioning children with ASD as compared to typically developing (TD) and developmentally delayed groups, suggesting that ASD may be associated with hyperactivity of the dopaminergic systems. While treatment success has been reported for dopamine blockers, definitive evidence regarding dopaminergic abnormalities in ASD is unavailable (Lam et al., 2005). Objectives: To examine blink rates in a group of high-functioning children with ASD in an effort to further elucidate potential abnormalities in dopaminergic activity. Methods: Participants were 14 children with ASD and 11 age- and NVIQ-matched TD children. Blinks were recorded during an Embedded Figures Test (EFT) using a binocular eye-tracking system. Time was divided into task (from trial onset until participant response) and inter-stimulus interval (ISI; from participant response until subsequent trial onset) for analysis of blink rates. Results: In the EFT, significant findings included a main effect of group and a condition (task, ISI) by group (ASD, TD) interaction. The ASD group had significantly higher blink rates than the TD group during the ISI, though not during task. Conclusions: Our findings show increased blink rate during task-free periods, which may suggest increased dopaminergic activity in children with ASD.

105.63 63 Diminished Variability of Neural Circuits in Autism: MEG Studies of Tactile Evoked Response. M. A. Coskun[1], S. L. Reddoch[2], D. A. Pearson[3], K. A. Loveland*[3], E. M. Castillo[2], A. C. Papanicolaou[2] and B. R. Sheth[1], (1)*University of Houston*, (2)*Univ. of Texas Med. Sch. at Houston*, (3)*University of Texas Medical School at Houston*

Background: A consensus is rapidly emerging that atypical neural connectivity is a central characteristic of the autism phenotype. However, there is far less consensus as to what exactly is atypical about the circuitry. One proposal is that the neural circuits of persons with autism are noisy or highly variable. Imbalance in the excitation/inhibition ratio and suppression of cortical inhibition support the hypothesis of noisy synapses. Empirical tests of this influential theoretical proposal are required.

Objectives: The noisy synapses hypothesis predicts reduced reliability or increased variability in the evoked responses of ADs. We tested this prediction by examining, in the brains of individuals with autism, the response to tactile stimulation using magnetoencephalography (MEG). To further dissect the precise nature of the putative difference in variability in individuals with autism versus control, we also examined the evoked MEG responses to touch of individuals with spina bifida and elderly controls.

Methods: Using a whole-head neuromagnetometer containing an array of 248 gradiometers in a MEG recording setup, we recorded the neural response to passive tactile stimulation of the thumb (RD1) and index finger (RD2) of the dominant hand of young adult control participants (17 high-functioning persons with autism and 18 typically developing persons, matched for gender and age) while they remained awake in an eyes-closed supine posture. We also used data recorded from 21 individuals with spina bifida (Myelomeningocele) and 8 elderly control participants, obtained under similar stimulation and recording conditions as for the autism group. We measured the mean and variability of the evoked response to tactile stimulation in all four groups. For each participant in our sample, the sensor in the contralateral somatosensory cortex that exhibited the largest evoked response relative to baseline was automatically selected. For this sensor, we computed across all trials and times (40-275ms following stimulus onset; 290 Hz sampling rate) for each body part the a) mean evoked response, b) variance in the evoked response, and c) the ratio of the variance to the mean of the response, a measure that is analogous to Fano factor.

Results: The evoked responses to tactile stimulation were less, not more, variable in the brains of persons with autism as compared to control ($p<<0.001$). The evoked responses of the spina bifida group was significantly less variable as compared to both controls as well as persons with autism ($p<<0.001$). The responses in the elderly controls were significantly less variable than those of the young adult controls ($p<<0.001$), whereas no difference was observed in comparison with the autism group ($p>0.1$).

Conclusions: The results thus far run counter to the hypothesis of noisy synapses in autism. Rather, diminished variability of neural response in autism and in other groups could be what distinguishes atypical brains from those of young, healthy control individuals.

105.64 64 Subliminal Perception of Emotional Faces in Autism. C. M. Hudac*[1], J. M. Arizpe[2], S. M. Lee[1], B. C. Vander Wyk[1] and K. A. Pelphrey[1], (1)*Yale University*, (2)*National Institute of Mental Health, National Institutes of Health*

Background: Neuroimaging studies of face processing in autism have reported hypoactivation within the lateral fusiform gyrus (FFG), ventrolateral prefrontal cortex (vlPFC), and the amygdala (Schultz et al., 2000; Dalton et al., 2005; Pinkham, et al. 2008). Hadjikhani et al. (2006) have suggested that hypoactivation in these regions are driven by a lack of attention to faces as well as abnormal scanpaths. These findings suggest that the face processing system is present in individuals with autism, but is not automatically engaged during free viewing. The question thus arises: What is the neural basis of abnormal visual scanpaths to faces in autism? Work in typically developing individuals has reported that the amygdala responds to fearful faces even in the absence of conscious perception (i.e., when emotional faces are backwards masked), as well as the lateral FFG, amygdala, and vlPFC (Whalen et al., 1998; Morris, Pelphrey, McCarthy, 2007).

Objectives: We sought to evaluate the hypothesis that responses to subliminally presented, emotionally expressive faces in the amygdala, FFG, and vlPFC would be abnormally low in individuals with autism. Prior evidence indicates that brain activation observed in response to masked faces is more likely to reflect the initial activity of a face detector, similar to the process reflected by the N200 response recorded directly from the cortical surface in the FFG as compared to more traditional FFG activations measured via fMRI during longer, unmasked stimulus presentations that are strongly influenced by top–down processes including attention, familiarity, and visual scanpaths (Allison et al., 1994; Wojciulik, Kanwisher, & Driver, 1998; Henson, Shallice, & Dolan, R, 2000).

Methods: To date, 7 rigorously characterized adult participants with high-functioning autism and 6 age-, IQ-, and gender-matched neurotypical controls participated in an fMRI study. In this rapid event-related design, images of standardized emotional faces (40 trials each of angry, disgust, fear, happy, and neutral) were presented for 15 ms and immediately masked by black and white mosaic images. Stimulus and mask presentations were followed by a jittered intertrial interval lasting from 2-5 s. Participants were asked to fixate a crosshair placed in the middle of the screen at all times. To ensure they maintained attention, participants were asked to press a button when a green mosaic infrequently appeared.

Results: A random-effects comparison of activity in response to the fearful faces revealed greater activity for the neurotypical group compared to the autism group in the FFG, amygdala, and vlPFC (t=3.42, p<0.001133, q<0.05). The same comparison for the response to facial expressions of disgust revealed neurotypical > autism activity in the FFG and insula (t=3.27, p<0.001777, q<0.05).

Conclusions: Consistent with prior work, we observed hypoactivation of key components of the face processing system including the amygdala, FFG, vlPFC, and insula. This study extends prior work by more precisely characterizing the level of dysfunction in this brain system in demonstrating dysfunction in a signal that has been linked to face detection. We conclude that disruption in face detection (seeing a face as a "face") might underlie atypical scanpaths in autism.

105.65 65 Integration of Autonomic Cues during Decision Making: Electrodermal Response by Young High Functioning Children with ASD While Gambling. S. Faja*[1], M. Murias[1] and G. Dawson[2], (1)*University of Washington*, (2)*Autism Speaks, UNC Chapel Hill*

Background: To date, there have been no published investigations of electrodermal response (EDR) during the Children's Gambling Task, and

investigation of EDR among individuals with autism spectrum disorders (ASD) has focused primarily on older children and adults. EDR during the gambling task has been sensitive to brain damage in the amygdala and ventromedial prefrontal cortex among adults (Bechara et al., 1996, 1999; Tranel et al., 2002), thus this approach provides a way to assess for early differences in neurodevelopment of children with ASD.

Objectives: To test whether young, high-functioning children with ASD respond differently to feedback (wins/losses) compared with age and IQ-matched controls. And, to test whether children with ASD are able to use autonomic information to guide their subsequent decision-making behavior between a risky and safe deck.

Methods: Subjects were 21 6 and 7-year-olds with ASD and 21 age and IQ-matched controls. Diagnosis was confirmed with the ADOS, ADI-R and DSM-IV-TR. All children in both groups had cognitive ability in the average to above average range (measured by the Differential Ability Scales). EDR data were collected during a 2-minute baseline period and while children completed the Children's Gambling Task (Kerr & Zelazo, 2004). Each trial included three 3-second events: anticipation of the card selection, response to positive feedback, and response to negative feedback. The dependent variable was the amplitude of the largest fluctuation in EDR for each of the 3 second event-related periods that were measured.

Results: There were no significant group differences in the amplitude of EDR during baseline. Overall, groups did not differ in the amplitude of their responses during the win or loss conditions. Nor, did they differ in their pattern of responding across the win and loss conditions, when a repeated measures ANOVA was used to test the interaction of group by feedback condition. Because the number of losses varied from card to card, children sometimes lost no treats and sometimes lost 1, 4, 5, or 6 treats. Responses to *actual* losses – when 1 or more treats were taken away – were examined separately and differed by group, $t(21.1) = 2.24$, $p = .04$. Children with ASD had significantly larger fluctuations in response to losses than controls, M=0.835 versus M= 0.484. EDR during the anticipatory period was then examined, and there were no group differences in overall amplitude or for risky or safe decks during the anticipatory period. Last, there were no significant correlations with advantageous selections on the Children's Gambling Task and EDR when groups were examined together or separately.

Conclusions: Children with ASD responded differently to negative feedback. Second, although children with ASD and controls had similar EDR in anticipation of the decks, anticipation was not related to advantageous selections for either group. These findings are more consistent with differences in amygdala than ventromedial prefrontal function at this age.

105.66 66 Neural Effects Following Affect Recognition Training in Autism Spectrum Disorders. S. Bölte*[1], S. Schlitt[2], A. Ciaramidaro[3], A. Beyer[2], D. Hainz[2], B. Weber[2], V. Gapp[2], F. Poustka[4] and H. Walter[5], (1)*Central Institute of Mental Health*, (2)*Goethe-University*, (3)*University of Turin*, (4)*Department of Child and Adolescent Psychiatry, J.W. Goethe University*, (5)*University of Bonn*

Background: One of the most consistent findings in the neuroscience of autism spectrum disorders (ASD) is hypoactivation of the fusiform gyrus (FG) during facial affect processing. In addition, reduced activation of the amygdala (AMG) has been associated with emotion perception alterations in ASD Objectives: In this study, we examined whether computer-aided basic facial affect recognition training using the «Frankfurt Test und Training of Facial Affect (FEFA)» is associated with increased activation of the FG and AMG as well as specific and generalized behavioral gains in high functioning ASD. Methods: Eight FEFA training sessions lasting one hour each are applied over a period of five to six weeks by experienced clinicians. BOLD-fMRI changes in the FG and AMG are registered pre-post applying an event-related facial emotion detection paradigm. Additionally, a battery of cognitive and clinical measures is assessed at baseline, post training and follow-up. Results: Preliminary findings in 13 trained versus 13 matched untrained participants aged 15 to 30 years (mean age: ~ 20.5 y, mean IQ: ~ 105) show enhanced BOLD-fMRI signal changes in the FG and AMG during implicit facial affect processing pre-post FEFA training. Behavioral facial affect recognition measures yield high effect size improvements for tasks being identical and similar to FEFA training material, but only minor effects for more general emotion recognition and social cognition tests as well as

clinical measures. Conclusions: In contrast to a previous pilot study (Bölte et al., 2006), the present data indicate that circumscribed behavioral gains in basic facial affect recognition are indeed correlated with robust and expected neural activation changes in the FG and AMG. Nevertheless, on the behavioral level, of a lack of sufficient generalization of acquired affect processing skills was confirmed.

105.67 67 No Difference in Spatial Contrast Sensitivity Function (sCSF) Between Adolescents with ASD and Typically-Developing (TD) Controls. E. Milne*[1], H. C. Koh[1] and K. Dobkins[2], (1)*The University of Sheffield*, (2)*University of California, San Diego*

Background:

Individuals with Autism Spectrum Disorders (ASD) have been shown to exhibit enhanced processing of local aspects of visual stimuli (Plaisted et al, 1999). As local features of visual stimuli are mainly conveyed by high spatial frequency (HSF) information, and global configurations by low spatial frequency (LSF) information, it was speculated that individuals with ASD may possess relatively greater sensitivities to HSF versus LSF visual mechanisms (Deruelle et al, 2004). Consistent with this hypothesis, in a study that measured visual acuity as the smallest gap in a C-shaped stimulus that could be correctly located, it was reported that adults with ASD exhibit higher visual acuity, i.e. greater sensitivity to HSF, than typically-developing (TD) controls (Ashwin et al, 2008). However, another study that measured contrast sensitivities for a range of low to high spatial frequencies using Vistech contrast sensitivity charts (Vistech Consultants, 1988), reported no significant differences between participants with ASD and TD controls (De Jonge et al, 2007). Thus, it is still debatable whether there exists differential spatial frequency sensitivity in ASD individuals.

Objectives:

In the current study, we investigated differences in LSF versus HSF sensitivities between ASD and TD individuals using a more sensitive measure of spatial contrast sensitivity. This involved using psychophysical techniques to map out the entire spatial contrast sensitivity function (sCSF), allowing group comparisons of peak spatial frequency (the spatial frequency yielding highest contrast sensitivity), the peak sensitivity (the highest contrast sensitivity) and visual acuity (the highest spatial frequency detectable).

Methods:

Data were collected from 10 adolescents with ASD and 25 TD adolescents, matched on chronological age (mean=185 months) and non-verbal IQ (mean=107). The stimuli were static horizontal Gabor patches, formed by convolving luminance gratings (subtending 3.1x3.1°) with a Gaussian envelope (S.D.=0.5°), presented at 7 different SFs (0.5cpd, 2cpd, 4cpd, 8cpd, 12cpd, 16cpd, 20cpd). To obtain contrast sensitivities, on each trial, participants reported in which of two temporal intervals the stimulus was presented (centrally), and contrast was varied in a staircase paradigm. Double exponential curves were fit to the data for each participant to obtain their sCSF. Three variables of interest were extracted from the individual sCSFs: peak spatial frequency (peakSF), peak contrast sensitivity (peakCS), and highest spatial frequency detectable i.e. visual acuity (VA).

Results:

There were no significant group differences in peakSF ($t(df=33)=1.08$, $p=0.286$), peakCS ($t(df=33)=0.211$, $p=0.834$) or VA ($t(df=33)=0.749$, $p=0.459$).

Conclusions:

The results revealed typical processing of low and high spatial frequency information in adolescents with ASD. Differences between our results (typical VA in ASD) and those of Ashwin et al. 2008 (enhanced VA in ASD) might be explained by the different stimuli/tasks used in the two studies (gratings versus letters) or by the different ages (adolescence versus adults).

105.68 68 Autistic Traits and Visual Sensitivity to Human, Animal, and Object Motion. Z. Fermano*, M. D. Kaiser and M. Shiffrar, *Rutgers University*

Background: Autism Spectrum Disorder (ASD) is associated with difficulties in social behavior and gesture comprehension-two processes that depend upon the perception of other people's movements. This raises the question of whether ASD is associated with decrements in visual sensitivity to human movement. Past research indicates that observers with fewer autistic traits demonstrate greater visual sensitivity to human

movement than to object movement while observers with more autistic traits demonstrate equal visual sensitivity to human and object movement (Kaiser, Fermano, & Shiffrar, 2008). Such evidence is consistent with the hypothesis that ASD involves selective deficits in the visual analysis of socially relevant information. However, the movements of people and objects differ significantly along many non-social parameters including rigidity, frequency, predictability and degrees of freedom. Do previous results reflect low-level differences in stimulus complexity or high-level differences in social relevance? A new psychophysical study addressed this question by examining visual sensitivity to animal motion.

The presence of autistic traits varies continuously across clinical and non-clinical populations (Baron-Cohen et al., 2001). The Autism-Spectrum Quotient (AQ) measures the extent to which typically developing individuals exhibit autistic traits (Baron- Cohen et al., 2001). We compared visual sensitivity to human, animal, and object motion by typical observers and investigated the relationships between each participant's perceptual sensitivities and the magnitude of that participant's autistic traits as measured by the AQ.

Objectives: The goal of this work is to determine whether increases in the magnitude of autistic traits is associated with selective decreases in the ability to perceive other people's movements per se.

Methods: Fifty-four typical adult participants completed the AQ and a classic psychophysical measure of visual sensitivity to complex motion. Point light displays of a walking person, walking dog, and moving tractor were constructed from motion capture data. In a blocked design, these stimuli were presented coherently (present) or scrambled (absent) and hidden within dynamic point-light masks that inhibited the use of local motion processes. On each trial, participants reported with a button press whether the target stimulus was present or absent. No feedback was provided.

Results: Correlation analysis revealed that AQ score was most strongly associated with visual sensitivity to human motion ($r = -.30$, $p = .01$), less strongly associated with sensitivity to dog movement ($r = -.21$, $p = .06$) and not significantly related to visual sensitivity to object motion ($r = -.06$, $p = .33$). Thus, increases in autistic traits are associated with decreases in visual sensitivity to human motion in specific and biomechanical motion generally.

Conclusions: There is a significant relationship between the presence of autistic traits in typical observers, as measured by the AQ, and changes in visual sensitivity to other people's actions and, to a lesser extent, changes in visual sensitivity to the actions of animals, at least when they are performing actions that humans can also produce (e.g., walking). This supports the hypothesis that visual motion processes are meaningfully related to social abilities.

105.69 69 M and P Pathway Sensitivities and Their Contribution to Motion Processing in Adolescents with ASD and Adolescents with Siblings with ASD.

H. C. Koh*[1], E. Milne[1] and K. Dobkins[2], (1)*The University of Sheffield*, (2)*University of California, San Diego*

Background:

Children with Autism Spectrum Disorders (ASD) are known to exhibit deficits in visual motion processing (Dakin and Frith, 2005). Cortical motion processors receive input from sub-cortical magnocellular (M) and parvocellular (P) pathways, so these pathways could play a role in the motion deficit. Infant siblings of individuals with ASD have shown higher *relative* M versus P pathway sensitivities when compared to control infants (McCleery, Allman, Carver & Dobkins, 2007). This effect observed in siblings is a potential endo-phenotypic marker of ASD, suggesting that ASD may be associated with atypical M versus P functioning early in infancy. Children/adolescents with ASD have shown typical M pathway sensitivities (Bertone et al, 2005, Pellicano et al, 2005), with some evidence for impaired P pathway sensitivities (Davis et al, 2006). However, these studies only compared *absolute* M and P pathway sensitivities between groups. To date, no study of ASD has compared *relative* M versus P pathway sensitivities between children/adolescents with ASD and typically-developing (TD) children/adolescents. The extent to which atypicalities in one/both of these pathways could contribute to motion deficits in ASD has also not been investigated.

Objectives:

In this study, *relative* M versus P functioning in children/adolescents with ASD, as well as the strength of input from these pathways to motion processing were measured. Adolescents with siblings diagnosed with ASD (SIBS) were also

tested to explore the existence of an endo-phenotype.

Methods:

Data were collected from 19 participants with ASD, 19 TD participants and 12 SIBS participants, matched on chronological age (mean=180months) and non-verbal IQ (mean=107). For each participant, contrast sensitivity was obtained for moving luminance (light/dark) and isoluminant chromatic (red/green) sinusoidal gratings, in a detection (DET) task, and a direction-of-motion discrimination (MOT) task. *Relative* M versus P pathway sensitivity was indexed by the log ratio of contrast sensitivity of luminance versus chromatic gratings (L:C) in the DET task. *Relative* contribution of M and P pathway for motion processing was indexed by the difference in log DET/MOT sensitivity ratios for luminance and chromatic gratings (Diff-Ratio).

Results:

ASD participants exhibited overall lower contrast sensitivity than TD and SIBS participants for the MOT task but not for the DET task ($F(2,47)=3.67$, $p=0.033$). ASD participants and TD participants did not differ on L:C ratios. However, SIBS participants showed L:C ratios lower than those of TD and ASD participants ($H(2)=6.97$, $p=0.031$), which indicates that the SIBS participants possessed lower *relative* M versus P pathway sensitivities There were no group differences in Diff-Ratios.

Conclusions:

Impaired performance on the MOT task in the ASD participants confirms previous reports of motion deficits in ASD. Their comparable L:C ratios and Diff-Ratios with TD participants suggest that the motion deficit is not driven by atypical *relative* M versus P functioning, or atypical *relative* strength of M and P pathway input to motion processing. Finally, the lower L:C ratios in SIBS participants, which is in the direction opposite to that reported in infant SIBS (McCleery et al., 2007), may reflect a compensatory developmental mechanism in individuals who have a genetic pre-disposition for ASD.

105.70 70 Power and Coherence Abnormalities in Autistic Children: Insights into Local Processing and Long Distance Functional Connectivity. J. R. Isler*[1], K. M. Martien[2], P. Grieve[1] and M. Herbert[3], (1)*Columbia College of Physicians and Surgeons*, (2)*Massachusetts General Hospital-Harvard Medical School*, (3)*Massachusetts General Hospital*

Background: Autistics show a diminished ability to integrate complex information but enhanced perceptual processing abilities for a variety of simple sensory stimuli. fcMRI scans have shown diminished long distance functional connectivity between visual and frontal cortices in autistics but increased functional connectivity in thalamocortical circuits involving visual system. EEG power spectrum measures the amount of electrocortical activation in regional neural networks across brain wave frequencies. EEG coherence measures electrocortical synchrony of oscillatory brain rhythms between neural networks, which is hypothesized as a mechanism for functional connectivity. We sought to test the hypothesis that autistics would show increased power in primary sensory cortices during sensory stimulation but that the increase in power would be associated with decreased long distance coherence, and hence functional connectivity, between primary sensory cortices in right and left hemispheres. Objectives: To collect long latency flash visual evoked potentials in age-matched autistic and control subjects and to compare power spectrum and coherence patterns for the two groups in the primary visual cortex. Methods: Flash visual evoked potentials (VEP) were recorded from children (ages 5 to 8 yr) with autism spectrum disorders (ASD, n = 6) and from age-matched controls (n = 8) using high-density EEG recording. VEP power spectrum was determined from averaged wave forms over a 1000 ms time frame after the stimulus and coherence was computed between all channel pairs for each frequency band over the 1000 ms time frame after the stimulus. Analysis focused on primary visual areas. Results: Group comparisons showed increased spectral power in the ASD group, predominately over left occipital region, across a range of frequencies including the delta, alpha, beta, and gamma bands as well as the high gamma band above 80 Hz, suggesting increased activation of visual cortex in children with ASD over controls. Simultaneously, coherence between left and right visual areas was reduced in children with ASD in the delta and beta bands, with a trend toward reduction in the alpha band, suggesting reduced cross-hemispheric functional connectivity in children with ASD compared to controls. The fact that local EEG power increased

at the same time that cross-hemispheric coherence was reduced argues strongly that our coherence result indexes neural connectivity and is not a mere consequence of volume conduction. Conclusions: Taken together, these results support the view that children with ASD have hyper-responsive primary sensory cortices in the brain with reduced long distance inter-hemispheric functional connectivity and hence decreased inter-hemispheric integration within sensory processing systems. Hyper-responsiveness of the primary visual cortex may relate to fcMRI findings of increased thalamocortical connectivity in autism.

105.71 71 Patterns of Epileptiform Activity and Clinical Response to Steroid Therapy in Autism. J. D. Lewine*[1] and M. Chez[2], (1)*Alexian Brothers Medical Center*, (2)*Sutter Neuroscience Institute, Sacramento; UC Davis Medical Center*

Background: Magnetoencephalography [MEG] reveals that a high percentage of children with an autism spectrum disorder [ASD] demonstrate epileptiform activity within the peri-sylvian region. The peri-sylvian region has also been shown to be the primary epileptic focus in Landau-Kleffner syndrome [LKS], an acquired epileptiform aphasia characterized by continuous spike wave activity in slow wave sleep. Several studies have shown that high doses of steroids can suppress epileptiform activity in LKS and lead to improvements in language, so there is growing interest in the possibility that steroids can be of benefit in autism.

Objectives: The current study sought to determine if specific patterns of epileptiform activity are predictive of the quality of clinical response to high-dose steroid therapy in the ASDs.

Methods: MEG data were retrospectively reviewed for 36 children [ages 3-10] with autism spectrum disorders and epileptiform EEG abnormalities who had been treated with high-dose prednisone. In 22 cases the MEG data that were available for review had been obtained 2-6 months prior to initiation of steroid treatment. In the remaining 14 cases the electrophysiological data had been obtained 2-24 months following steroid withdrawal. Based on a blinded review of clinical notes, standardized tests [as available], and parental interview, 20 of the 36 children were classified as steroid responders.

Results: In the comparison of MEG data from responders versus non-responders, the most predictive information about treatment responsivity came from the actual pattern of epileptiform activity. Specifically, the highest predictive value was seen for the following rule -- 'Subjects with epileptiform activity restricted to peri-sylvian, inferior-frontal, and peri-Rolandic regions were likely to respond to steroids, whereas those with activity outside of these regions were unlikely to respond to steroids. This simple rule led to correct classification of 17/20 responders (85%) and 15/16 non-responders (94%).

Conclusions: A subset of children with ASDs and epileptiform activity show transient positive improvements in language when they are treated with steroids. Unfortunately, there is often a significant regression in skills following treatment withdrawal [as demanded by the development of medical side-effects], although some children do maintain improvements after medication taper. MEG patterns of epileptiform activity help to identify those children most likely to show transient positive benefits from steroid therapy. Best responses are seen for male subjects without clinical seizures for whom epileptiform activity is restricted to peri-sylvian, inferior-frontal, and/or peri-rolandic regions. The present data suggest that, for some children with autism, language compromise is associated with an active process that can be controlled by appropriate medical management, with MEG helping to identify those children most likely to benefit from aggressive intervention with steroids. Even though steroids are obviously not a good long-term treatment strategy for children with ASDs, a better understanding of how steroids can effect positive changes in some children may provide critical insight into the nature of autism and may lead to safer, more effective therapeutic interventions.

105.72 72 Head Circumference of Israeli Children with Autism Spectrum Disorder. M. Davidovitch*[1], D. Golan[1], O. Vardi[1], D. Lev[2] and T. Lerman-Sagie[2], (1)*Maccabi Healthcare Services*, (2)*Wolfson Medical Center*

Background:

An increased incidence of macrocephaly has been found among autistic children estimated at 20%. Brain development in autism shows accelerated growth in early life that results in brain enlargement in childhood. Based on this consistent finding in a subgroup of children with

autism, theories have been raised regarding the relationship between macrocephaly and the pathogenesis of autism.

Objectives: To evaluate the prevalence of abnormal head circumference of children with autism in one district of Israel and to compare it to the published data on autistic children, and to the head circumference of children with developmental language disorder (DLD).

Methods:

The head circumference of all children diagnosed with autism and Pervasive Developmental Disorder NOS (by DSM IV criteria) during 2000-2008 at the child development centers in the Shfela and Jerusalem districts of Maccabi Healthcare Services were searched from their computerised files. Only children with documented measurements were included. The measurement at the first evaluation was collected. Exclusion criteria were: severe neurologic deficits, genetic syndromes and S/P prematurity.

The control group included children diagnosed with DLD, with or without gross and fine motor delays. All children with DLD who were diagnosed during 2006-7, were included in alphabetical order to match the number of children with autism. An additional exclusion criterion was mental retardation.

Macrocephaly was defined as a head circumference >97th percentile and microcephaly as a head circumference <3rd percentile (Nellhaus head circumference charts, 1968).

Results:

296 children (250 boys [84.5%]) with autism met the above criteria. The mean age for head circumference measurement was 2 years and 8 months. Macrocephaly was found in 3.7% (P=0.7 NS) and microcephaly in 3% of children with autism.

299 children with DLD (228 boys [76.3%]) were included. Macrocephaly was found in 2.7% and microcephaly in 9.4% (P<0.0001). Mean age at their first measurement was 3 years and 10 months.

Conclusions:

The prevalence of macrocephaly among children with autism in Israel is similar to the expected in the normal population and in children with language impairment. The overall distribution of the head circumference measurements in autistic children is typical. The lack of a large subgroup of children with autism and macrocephaly suggests a possible different genetic background of Israeli children with autism. The unexpected proportion of children with DLD and microcephaly might reflect some undiagnosed genetic or environmental causes and should be further investigated.

Conclusions:

105.73 73 Heart Rate Variability and Electrodermal Activity in Children with Atypical Sensory Processing: Exploratory Pattern Analysis. E. Hedman*[1], M. Eckhardt[1], M. Z. Poh[1], M. S. Goodwin[2], L. J. Miller[3], B. Brett-Green[3], S. A. Schoen[3], D. M. Nielsen[3] and R. W. Picard[1], (1)*Massachusetts Institute of Technology, The Media Laboratory*, (2)*Massachusetts Institute of Technology*, (3)*Sensory Processing Disorder Foundation*

Background: Atypical sensory processing can cause significant functional impairment, and is widely reported in persons with autism. The Sensory Processing Disorder Foundation has designed and carried out carefully controlled experiments for eliciting and measuring Autonomic Nervous System (ANS) responses to six types of sensory stimuli (i.e., pure tone, auditory, visual, olfactory, tactile, and vestibular). Electrodermal activity (EDA) and heart rate variability (HRV) data have been gathered from a number of children with and without sensory processing problems while systematically exposed to these stimuli.

Objectives: We sought to evaluate how accurately various pattern recognition algorithms discriminate children with sensory processing challenges (SEN, n=34), including those with autism (n=21) and those with idiopathic sensory difficulties (n=13), from typically developing children (TYP, n=10) using EDA and HRV reactivity to the sensory stimuli mentioned above. We also evaluated which small set of features derived from raw EDA and HRV waveforms were most effective at distinguishing SEN and TYP in order to gain insight into what is different about autonomic responsivity in these two groups.

Methods: We started with 580 EDA and HRV features obtained from six different sensory stimuli (8 trials each) as well as rest (before the experiment) and recovery (after the experiment) periods. We employed an automated process to

find a smaller subset of features optimized for discriminating the SEN and TYP groups. The process cascaded two techniques – multi-class principal components analysis, followed by sequential floating feature selection. The features were first grouped into three different categories (524 of EDA; 56 of HRV; 32 of EDA + 56 of HRV), and used as input to the feature selection process, which was run with four powerful pattern classifiers: Linear Discriminants, K-Nearest Neighbor, Decision Trees, and Support Vector Machines. The process resulted in 12 different classifiers, each using an optimized set of features ranging in size from 3 to 57. These classifiers have the ability to distinguish complex high-dimensional patterns in multimodal data. We ran the twelve classifiers on data from 44 individuals (34 SEN, 10 TYP).

Results: We used leave-one-out cross-validation for training and testing each classifier on separate subsets of the data (leave out one person's data, train a model on the data from 43 people, then test the trained model on the person left out). Eight of the twelve classifiers achieved greater than 80% specificity and sensitivity in separating the SEN and TYP groups. Of these eight, two achieved this performance using 5 or fewer features. The Decision Tree with only 4 EDA features achieved 94% sensitivity and 80% specificity, while K-NN with only 5 EDA features achieved 88% sensitivity and 90%.

Conclusions: Across machine learning classifiers, we identified a relatively small subset of HRV and EDA features that separated the SEN and TYP groups. The discrimination ability of these features should be replicated on an independent sample. If findings are confirmed these features may serve as diagnostic criteria and intervention outcomes in the future. This poster will present the discriminatory methods, features, and detailed findings of the study.

105.74 74 Pupillary Response to Faces in Children with Autism. L. Sepeta*[1], N. Tsuchiya[2], M. S. Davies[1], M. Sigman[1] and S. Bookheimer[1], (1)*University of California, Los Angeles*, (2)*California Institute of Technology*

Background: Among the most prominent features of the social communication impairment in autism is the tendency to avoid direct eye contact with others. From a young age, children with autism look at faces less than typically developing children and tend to avoid eye contact, even with their primary caregiver. However, there is controversy over the reason for this reduced eye contact. Do they avoid eye contact because they experience the eyes of others to be aversive? Or, are they not motivated to look at eyes because they find the eyes uninteresting? Objectives: To investigate the underlying causes for this reduced eye contact and abnormal facial fixation behavior, we monitored gaze fixation and pupillary diameter as a measure of autonomic response in children with autism and age-matched typically developing children while they looked at human emotional faces. Methods: A group of high-functioning individuals with autism (n=20) was compared to a group of typically developing children (n=18) as they viewed faces displaying either happy, fearful, angry or neutral emotions. Subjects viewed faces in two conditions. In the "gaze-direct" condition, the eyes were gazing directly at the subject, while in the "gaze-averted" condition, the eyes were averted from the subject. Eye fixation crosses appeared before each face to cue gaze to the eye region. Using an infrared eye-tracking device, pupillary diameter and fixation patterns for each type of stimuli were compared within and between the two groups. Results: Overall, children with autism and typically developing children showed similar fixation behavior and pupillary responses; however, they showed marked difference in their pupillary response sensitivity to gaze direction for happy faces. Typically developing children showed increased pupillary diameter to happy faces with direct gaze compared to those with averted gaze ($p<0.05$), whereas children with autism did not show such sensitivity to gaze direction for happy faces ($p>0.05$). Of potential concern is whether or not these pupillary response differences could be secondary to differences in fixation behavior; however, for happy faces, fixation duration did not correlate with modulation of the pupillary response by the gaze direction across both groups for any of the regions (R2 all below 0.073, $p>0.1$). Thus, there was no systematic relationship between fixation behavior and the pupillary gaze effects. Conclusions: We interpret the increased pupillary diameter to happy faces with direct gaze in typically developing children to reflect the intrinsic reward value of a smiling face looking directly at an individual. The lack of this effect in children with autism is consistent with the hypothesis that throughout development, children with autism are less motivated to look at the eyes and face because of impaired processing of social reward. We hypothesize that the failure

to attach a reward value to social stimuli in the individuals with autism early in the development may result in weaker motivation to look at faces. In turn, this may hinder the development of neuronal circuits specialized for processing faces, and more broadly lead to a cascade of negative consequences for social development.

105.75 75 Pre-Pulse Inhibition: Its Expanded Use in Differentiation of Autism Caused by Fragile X Syndrome Versus Idiopathic Autism. J. Yuhas[1], L. Cordeiro[2], A. Schneider[1], E. Ballinger*[2], R. Hagerman[3] and D. Hessl[2], (1)*University of California, Davis*, (2)*M.I.N.D. Institute, University of California at Davis Medical Center*, (3)*UC Davis*

Background: Pre-pulse inhibition (PPI) of the eyeblink startle reflex in response to auditory stimuli has been shown to be reliably indicative of sensorimotor gating deficits in fragile X syndrome (FXS). In addition, PPI deficit rescue has been linked to the pharmacological use of mGluR5 antagonists. As such, PPI has become an important quantitative outcome measure for FXS targeted treatment studies. Prior literature suggests that idiopathic autism and autism caused by FXS share a common pathophysiological etiology, though few studies have directly compared these two groups. Some individuals with idiopathic autism have demonstrated sensorimotor gating deficits similar to those seen in FXS, which could be quantitatively measured through the PPI protocol and perhaps explained through the theory of shared neurobiology.

Objectives: To compare the PPI profiles in individuals with idiopathic autism with those of the individuals with autism caused by FXS in order to further characterize their neurobiology, which may important implications for future pharmacological interventions (particularly the use of mGluR5 antagonists) in autism.

Methods: PPI was compared in age- and IQ-matched groups with FXS and autism (FXS+A), FXS without autism (FXS-A), idiopathic autism confirmed negative for fragile X (IA) and controls. In addition, a Repetitive Behavior Scale, a Short Sensory Profile and cognitive measures were collected from each subject.

Results: The FXS-A group had lower PPI compared to controls ($p < 0.001$), as did the FXS+A group ($p < 0.05$). The FXS-A group had lower PPI than the IA group ($p < 0.05$). The PPI difference between the FXS+A group and the IA group approached statistical significance, with the FXS+A group having lower PPI than the IA group. There were no other significant differences in PPI among other comparison groups, including the comparison between the two FX groups and the comparison between the IA group and the controls. PPI did not significantly correlate with any of the behavioral measures administered. Conclusions: The significant difference between the FXS-A and the IA groups and the trend towards significance between the IA and FXS+A groups suggest that the presence of FXS may be the driving force behind a sensorimotor gating deficit in these comparisons. As such, the underlying physiological mechanism of sensorimotor gating may not be common between individuals with FXS (with or without autism) and individuals with IA, so PPI may be a valuable tool for distinguishing autism that is due to FX from other etiologies. However, the IA sample size is small, and given the heterogeneous nature of IA, greater numbers are needed to validate these conclusions. Nonetheless, these results, when combined with recent findings linking PPI to the mGluR5 theory and neurobiology of FXS, support the potential of PPI to be an important outcome measure in testing the efficacy of targeted treatments for FX and other neurobiologically-related populations.

105.76 76 Executive Function Deficits and Emotion Recognition Problems In Boys with Klinefelter Syndrome, Related to Social Dysfunction and Autism. H. Swaab*[1], H. Bruining[2], S. Van Rijn[3], M. Bierman[1], H. van Engeland[2] and L. de Sonneville[1], (1)*University of Leiden*, (2)*University Medical Centre, Rudolf Magnus Institute of Neuroscience*, (3)*Leiden University*

Background:

Klinefelter syndrome, determined by a XXY chromosomal pattern, affects approximately 1 in 700 male individuals and is the most common sex chromosomal disorder. Apart from a variety of phenotypes, like hypogonadism, androgen deficiency and infertility, cognitive and behavioral dysfunctions are recognized to be associated with this chromosomal pattern. Especially social dysfunction is reported. Shyness, high levels of social anxiety, social impulsiveness and social withdrawal have been found in Klinefelter man. High levels of autism traits in men with Klinefelter syndrome were reported by our group, findings that draw even more attention to the vulnerability for social dysfunctions associated with Klinefelter syndrome. Studies so far mainly focus on adult populations and data about the social development of boys with Klinefelter syndrome

are scarce, although recent studies of our group revealed 25% autism related disorders in boys with Klinefelter.

Objectives:

We addressed the question whether children with Klinefelter syndrome have EF problems and problems in social cognition that are associated with social problems and autism symptoms. The EF domains of attention regulation, inhibition and mental flexibility, were evaluated as well as the social cognition domains recognition of faces and the ability to recognize emotional expressions on faces.

Methods:

56 boys with Klinefelter syndrome (mean age 10.7) were compared to a group of 112 normal control boys, matched on age. Social dysfunction and autism symptoms were measured by the Child Behavior Checklist (CBCL) and the Autism Diagnostic Interview (ADI). Attention regulation was measured by a classic Continuous Performance Task (CPT), inhibition of processing of irrelevant information was indicated by the proportion of impulsive responses (misses) on the CPT. Mental (in)flexibility was indicated by the score on the incompatible respons on a set shifting task (SS-VIS) task. In addition, tasks of face recognition and facial emotion recognition were used as measures for social cognition.

Results:

35% of the Klinefelter population had scores above the clinical cut-off point on the social problem scale of the CBCL. 25% of the children did meet the criteria for autism on the ADI. Attention regulation was less well developed in Klinefelter boys (p=.000). Klinefelter boys showed much difficulty in inhibition of responses (p=.000) and their mental flexibility was less well developed (p=.000). Boys with Klinefelter were less accurate in recognition of faces (p=.001). They also had much more difficulty in fast and accurate recognition of emotional facial expression (p=.000).

Conclusions:

Boys with Klinefelter syndrome show difficulty with attention regulation, inhibition, and mental flexibility. These EF functions are known to be essential in regulation of thought and behavior, especially social adaptive behavior. Therefore, social adaptive problems in Klinefelter and autism symptoms, might be associated with less well developed EF. Moreover, children with Klinefelter syndrome appeared to have difficulty in recognition of faces and facial emotions, which is associated with social dysfunction as well.

105.77 77 Lack of Emotion-Specific Facial Mimicry Responses among High-Functioning Individuals with An Autism Spectrum Disorder. A. Rozga*, M. Mumaw, T. King and D. L. Robins, *Georgia State University*

Background: Previous research has shown that presentation of facial expressions of emotion automatically evokes subtle changes in the observer's facial muscle activity as measured with electromyography (EMG), with differential muscle activity evoked depending on the affective valence of the stimulus. This phenomenon, termed facial mimicry, is hypothesized to represent a psychophysiological mechanism of emotion perception and empathy, and as such, may be a good biological marker of a disruption to the emotion perception system among individuals with Autism Spectrum Disorders (ASD).

Objectives: To examine automatic facial mimicry to happy and angry expressions of emotion among high-functioning individuals with ASD and a typically developing control group utilizing dynamic audiovisual stimuli.

Methods: Participants included nine high-functioning individuals with a diagnosis of ASD (mean CA = 20.2 yrs) and 15 typically developing controls (mean CA = 14.6). There were no significant differences between the groups with respect to chronological age, verbal and nonverbal IQ, and face recognition. Participants underwent a dynamic emotion perception task during which they judged the emotion expressed in 2-second video clips containing facial expressions and affective prosody while EMG sensors recorded facial movements on zygomatic (cheek) and corrugator (brow) muscles. Analyses focused on within-group comparisons of average levels of left zygomatic and corrugator muscle activity, 500ms to 1000ms post stimulus onset, between happy and angry stimuli.

Results: As expected, for the control group, happy stimuli elicited significantly more zygomatic activity than did the angry stimuli [t(14) = 2.98,

$p < .01$, partial $\eta^2 = .39$], and angry stimuli elicited a trend toward more corrugator activity than the happy stimuli [$t(14) = 2.06$, $p = .06$, partial $\eta^2 = .23$]. In contrast, there were no differences in corrugator and zygomatic activity in response to either angry or happy stimuli among the ASD participants (all ps > .1).

Conclusions: Preliminary results of our analysis of EMG response to dynamic facial expressions and affective prosody suggest that unlike typically developing individuals, individuals with ASD do not show an emotion-specific differential EMG response. In this regard, our findings tentatively echo those of McIntosh and colleagues (2006), who found that participants with ASD failed to demonstrate significantly more congruent than incongruent facial EMG responses to static photographs of happy and angry facial expressions. These findings raise the question of whether disrupted facial mimicry may be a psychophysiological substrate underlying previously documented impairments in emotion recognition and emotional responsiveness among individuals with ASD. Consequently, in future analyses with a larger sample, we will examine group differences in patterns of EMG activity and latency to EMG response, and we will explore whether disruptions in facial mimicry have implications for social-emotional functioning among individuals with ASD.

105.79 79 Electrophysiological and Behavioral Investigation of the Processing of Visual Stimuli in Infants at Risk for Autism Spectrum Disorders. V. Vogel-Farley*[1], T. Augenstein[1], J. Y. Yim[2], C. A. Nelson[1], H. Tager-Flusberg[2], L. M. Casner[3] and L. M. Kasparian[2], (1)*Children's Hospital Boston*, (2)*Boston University School of Medicine*, (3)*Boston University*

Background:
One of the most exciting and rapidly evolving areas of research on ASD is the identification of risk markers that can be identified in the infancy period. Zwaigenbaum et al. provide the rationale for employing prospective longitudinal designs of infants at risk (basis of an older diagnosed sibling), an approach that is now being followed by a growing number of research groups. At 9-10 months, differences between high and low risk infants were found in visual disengagement, and in response to direct and averted eye gaze (Elsabbagh et al., in press a, b) using eye-tracking and ERP measures.
Objectives:
We are investigating differences in neurobehavioral markers of risk in visual processing systems that can be detected between 6 and 12 months. This is a highly significant developmental stage because during this time development of both language and social perception depend on critical socially-embedded learning experiences. Our research program focuses on identifying neurobehavioral indices of social attention as well as general measures of cognitive and brain development using a combination of behavioral, eye-tracking and neurophysiological (EEG; ERP) measures.
Methods:
In the current project we employ high-density event-related potentials (ERPs) and eye tracking to examine risk-markers for ASD among infants at high risk for autism (HRA) (by virtue of having one affected sibling). Infants are being studied at 6, 9 and 12 months. Using ERPs and eye tracking, we are examining the processing of mother vs. stranger.
Results:
On the ERP data we have collected to date we conducted statistical analyses. At 6 months, the peak amplitude for the N290 yielded a significant group x region interaction; similar findings were obtained for the mean amplitude. We also analyzed the Nc and at 6 months there was a significant group x person interaction for latency: the low risk group latencies were shorter to the mother, whereas the HRA group latencies were shorter to the stranger; latencies for this group were overall, longer. Behaviorally, the infants with preliminary diagnostic outcomes of ASD look proportionately less at their mothers at both 6 and 9 months. No significant effects were found at 12 months. The second figure shows the proportion of time looking at the eyes at 6, 9, and 12 months. The infants with ASD preliminary outcomes show a sharp decline in time spent looking at the eyes between 9 and 12 months. Reduced attention to the eyes in the HRA infants is consistent with findings from other labs.
Conclusions:
These data suggest that there are interesting group differences at 6 months in brain regions processing, and in neural markers of attention to familiar and unfamiliar faces. We speculate that the absence of group effects at 12 months may be the result of increased heterogeneity in the neurophysiology of face processing in the HRA infants.

105.80 80 Social ABCs for Toddlers with Autism: Evaluation of a Parent-Mediated Intervention. J. Brian*[1], I. M. Smith[2], T.

McCormick[3], E. Dowds[1], C. Sauve[3], K. Smith[3], D. Ostfield[4], L. Zwaigenbaum[5], W. Roberts[6] and S. E. Bryson[2], (1)*Bloorview Kids Rehab and Hospital for Sick Children/ University of Toronto*, (2)*Dalhousie University/IWK Health Centre*, (3)*IWK Health Centre*, (4)*McGill University*, (5)*University of Alberta*, (6)*University of Toronto*

Background: Progress in identifying the earliest signs of autistic spectrum disorder (ASD) through prospective studies of high-risk infants has raised the question of whether intervention provided at such a young age could mitigate compromised developmental trajectories. We are addressing this need by evaluating our newly-developed '*Social ABC's*' intervention. This parent-mediated intervention is informed by emerging prospective data on early impairments in ASD, as well as evidence-based principles of Pivotal Response Treatment (PRT) for enhancing development in ASD (Koegel & Koegel, 2006), and the broader literature on effective parent training for infants at high risk for sub-optimal outcomes (e.g., Landry et al., 2001). Adaptation of PRT for younger children also draws on recent evidence of the effectiveness of parent training in PRT for newly diagnosed 3- to 4-year-olds with ASD (Coolican, 2008).

Objectives: The main aims were to (1) describe our newly developed *Social ABC's* intervention model and (2) present data from our first 4 pilot families regarding fidelity of implementation and child outcome variables. Methods: In our pilot study, we have trained interventionists to fidelity both in implementing the intervention techniques and in training parents as implementers; established the feasibility and acceptability of our program to parents; manualized our treatment model and refined it based on parental feedback; tested and refined our behavioural coding schemes; and finalized our choice of outcome measures and established their sensitivity to changes both in toddlers with ASD and their parents.

Results: After describing our 24-week intervention model, we report on data regarding (1) interventionists' fidelity in implementing PRT and in training parents (having achieved > 80%), and (2) parents' fidelity of implementing the intervention techniques. A case series will demonstrate child gains in (1) functional communication skills (e.g., responsivity to verbal models, coded from video), and/or in (2) cognition, language/communication, and/or autistic symptoms (on standardized measures). Preliminary analyses show that three of four infants demonstrated reductions (i.e., less atypicality) in ADOS Communication scores (changes of 1, 2, and 3 points, respectively). The Mullen Scales of Early Learning/ Preschool Language Scales-4 captured improvements in Receptive Language for three cases (gains of 22, 26, and 36 T score points), and an Expressive Language gain in two children (16 points each). Negligible changes in T scores were noted for non-targeted Visual Reception or Gross/Fine Motor domains with only one exception (+13 T score points for VR in one case). Despite some variability in outcomes, gains are reported in all parents with respect to fidelity of implementation, and in all children on at least some variables of interest.

Conclusions: This is a user-friendly, highly practical and promising intervention for high-risk toddlers. The program is manageable and feasible for parents, and they are able to become highly skilled in the intervention techniques. Although individual variability exists in parent fidelity and child gains, we provide evidence of language-specific gains in high-risk infants using this intervention. Intervention provided by parents this early in life holds significant promise for minimizing, if not preventing, some of the most disabling features of ASD.

105.81 81 Outcomes of Two-Year-Olds Enrolled in a Comprehensive Developmental Intervention. R. Landa*, *Kennedy Krieger Institute*

Background:

Early intervention for children with ASD has been a public priority. However, there has been little empirical data available to judge the potential impact of early intervention on later functioning.

Objectives:

To examine change in cognitive functioning over the course of one to six years after enrollment into an early intervention study in a group of 2-year-olds.

Methods:

Forty nine children who had entered an early intervention study between the ages of 24 and 33 months of age were tested one to six years after the onset of the intervention. The children had

received 10 hours per week of center-based intervention within a classroom setting for a period of 6 months. Multiple intervention strategies were employed. A comprehensive curriculum was used. Weekly parent education sessions were provided, and monthly home visits were made to train parents on core intervention goals within the home. Children were assessed with the Mullen Scales of Early Learning prior to entry into the intervention, at the end of the intervention, and at a 6-month post-intervention follow-up. Sixteen of the children have thus far completed another follow-up assessment at 4, 5, 6, 7, and/or 8 years of age. Six of these children completed the Mullen, and 10 completed the Stanford Binet V at the second follow-up assessment. Dependent variables examined here included nonverbal functioning (Mullen Visual Reception T score; Stanford Binet Nonverbal IQ), verbal functioning (Mullen Receptive and Expressive T score; Stanford Binet Verbal IQ), and overall cognitive functioning (Mullen Early Learning Composite; Stanford Binet IQ). Assessments were conducted by expert clinicians blind to intervention status and to children's pre-intervention level of functioning. Children were tested in an unfamiliar environment with materials that were not used in the intervention classroom.

Results: Forty five percent of participants (n=22) made robust and sustained improvement from the pre-intervention to follow-up assessment that resulted in a shift from impaired functioning (scoring >1.5 sd below the mean) to functioning within normal limits (within 1 sd of the test mean). For example, the mean Mullen Expressive Language T score improved from 26 (>2 sd below mean) to 46 (within 1 sd of the mean) in this group of robust responders. Nonverbal functioning improved from impaired at the pre-intervention assessment (e.g., mean Mullen Visual Reception T score of 33, more than 1.5 sd below the test mean) to age-appropriate at follow-up (e.g., 44, within 1 sd of the mean). Overall cognitive functioning (based on a mean of 100, sd=15) improved from a mean of 62 at pre-intervention to 96 at the follow-up assessment. This represents improvement that was sustained at least 6 months after the intervention was terminated. An additional five children made robust improvements in nonverbal or verbal functioning but their scores fell short of age-appropriate levels. Other children made improvement but did not reach age-appropriate levels on these measures.

Conclusions:

These findings indicate that comprehensive intervention initiated at 2 years of age for children with ASD may lay the foundation for important developmental gains in nonverbal and verbal aspects of functioning.

105.82 82 Utilizing Social Stories for Behavior Change in Preschoolers with Autism. L. A. Wright* and R. McCathren, *University of Missouri*

Background: Autism is a neurological disability that is diagnosed in increasingly large numbers of children, which necessitates effective intervention strategies for practitioners. A teaching intervention of increasing popularity used to increase pro-social behavior and decrease problem behavior in young children with autism is Social Stories™.

Objectives: The objective of this study was to evaluate the effects of a Social Story™ intervention on the social behavior rates of 4 young children with autism including the following research questions:

In preschoolers with diagnoses of autism:

(1) Does Social Story intervention increase socially appropriate behavior and decrease problem behavior?

(2) Do the social behavior rates approach those of age and gender-matched typically developing peers?

(3) Are the effects of intervention maintained over a one month period?

(4) Do teachers support the social validity of Social Stories?

Methods: This study used a multiple-baseline across participants design to evaluate the effects of the Social Story on the pro-social and problem behaviors of each of the participants in comparison to gender and age-matched peers in the inclusive preschool classroom.

Results: The results of this study indicate that the Social Story was effective in increasing pro-social behavior rates in 3 of the 4 participants, though none of the participants reached the pro-social behavior rates of age and gender-matched peers. The problem behaviors of all 4 participants decreased with the intervention. Maintenance of skills over a 1-month period was demonstrated for all of the participants.

Conclusions: The present research adds to the

current small though growing literature base in support of the use of Social Stories. Due to the call for scientifically based research in the classrooms, this study contributes to the support of Social Stories as an evidence-based practice for recommended use by practitioners in the field.

105.83 83 A Pilot Study on the Implementation of a Joint Attention, Parent Training Package, for Parents of Preschool Age Children with Autism. S. Ferguson*, *University of Canberra (ACT)*

Background:

By the end of the first year of life typically developing infants are not yet able to speak clear words, yet they have mastered the building blocks of social communication, they can coordinate attention between people and objects, and communicate with caregivers in intentional ways, using vocalizations and gestures that have shared meanings. They have developed joint attention. One of the earliest emerging deficits in children with autism is their lack of these joint attention skills. This has been shown not to improve over time without intervention. Several studies have successfully taught joint attention skills to young children with autism, using behavioural techniques, play based approaches, and combined approaches. Both children and their parents have been targeted in these studies, as teaching parents helps to generalize the skills into the child's everyday life. More studies are now needed to translate the findings of this research into practice.

Objectives:

This purpose of this pilot study is to examine the efficacy of a joint attention training package using both behavioural and transactional approaches. Several parent teaching techniques are being used, psycho-educational, live modeling and coaching, and video coaching. Parents will be asked to evaluate the usefulness of these approaches.

Methods:

This pilot involved one child, diagnosed with autism, who was 4years and 3 months, and their family in a single subject design. The continuous measure was a semi structured, play based, videoed observation which was coded for a range of joint attentional behaviors. 35 sessions were run, over a 3 month period, both in a university laboratory, and in the home. Sessions involved both adult led table based activities, and child led floor based activities. Pre and post assessment measures included the Autism Diagnostic Observation Schedule, (ADOS), module 2, the Early Social Communication Scales, (ESCS), Performance and General Language subtests from the Wechsler Preschool and Primary Scale of Intelligence III, (WPPSI III), The Adaptive Behavior Assessment System II, (ABAS II), the Clinical Evaluation of Language Fundamentals Preschool -II (CELF P II), and the Parenting Stress Index, (PSI). A parent satisfaction and feedback questionnaire was administered at the end of the intervention.

Results:

Coding of the continuous measure videos is currently underway, and post intervention assessment currently being undertaken. Preliminary results indicate significant changes in child joint attention behaviours and a high degree of parent satisfaction with the intervention. Data and analyses will be available for presentation at the conference.

Conclusions:

This pilot has provided good support for the main study to be conducted in 2009 with 6 families. The findings of the pilot study will inform the final design of the parent teaching package. The research design of the main study will also be single subject, but will use a multiple baseline across subjects replication. More detailed conclusions will also be available, for presentation at the conference, when the data for this pilot is analysed.

105.84 84 Joint Attention Intervention in the Preschool – a Randomized Study. A. Kaale*[1], E. Sponheim[1] and L. Smith[2], (1)*Ullevaal University Hospital*, (2)*Centre for Child and Adolescent Mental Health*

Background: Young children with autism experience severe difficulties in joint attention (JA), and their ability to initiate and respond to JA is associated with social engagement and later language skills. Recent JA-intervention studies have shown promising results. However, there is a need to investigate the effectiveness of JA-intervention when it is moved from the University clinic in to the mainstream preschool.

Objectives: The present study investigates the possible improvement in joint engagement in

children with autism following a JA-intervention implemented in mainstream preschools.

Methods: Sixty one children diagnosed with autism (age 24 to 60 months (mean CA=48 months, range 29-60) were randomly assigned to a JA intervention group (n=34) or a control group (n=27). The intervention was based on an adaptation of the JA-intervention method developed by Connie Kasari at UCLA. Children in both groups continued their regular programs while the children in the intervention group also participated in two daily JA-intervention sessions for a period of 8 weeks (total of 26 hours of intervention). The sessions were done in the preschool by preschool teachers or aids receiving weekly supervision by trained counselors. For this part of the study participants were videotaped during 10 minutes of free play with their mother with a standard set of toys at pre- and post-treatment. The videotapes were then coded for six different engagement states (Bakeman and Adamson; 1984, 2004).

Results: Videotapes are now in the process of being coded. Preliminary findings from 33 children indicate that children randomized to the JA-intervention group evinced a higher proportion of time in joint engagement compared to children in the control group at post-test (intervention group 62% and control group 50% of the time spent in joint engagement). Data for the entire sample with control for pre-test measures will be presented at the conference.

Conclusions: It is important to investigate whether intervention targeting JA implemented within mainstream preschools yields beneficial outcome for young children with autism. This study provides information about this question.

105.85 85 Developmental Associations Between Attention, Language, and ASD Symptomatology in the Infant Siblings of Children with Autism Spectrum Disorders (ASDs). L. Ibanez*, C. Grantz, W. Gealy, M. Kimijima and D. S. Messinger, *University of Miami*

Background:

Children with Autism Spectrum Disorders (ASDs) exhibit deficits in their ability to disengage and shift visual attention. They also show deficits in their ability to initiate joint attention (IJA), which in typically developing populations is associated with later language development. The infant siblings of children with an ASD (ASD-sibs) show similar impairments when compared to the infant siblings of typically developing children (COMP-sibs). Few studies have examined how these early deficits relate to one another and to later ASD symptomatology in ASD-sibs.

Objectives:

This study examined the developmental associations between early visual attention, joint attention, language development, and ASD symptomatology in ASD-sibs and COMP-sibs.

Methods:

In the Face to Face-Still-Face Protocol (FFSF) at six months, parents were instructed to play normally with their infant, hold a still-face, and then resume play. Visual attention was measured as the frequency of infants' gaze shifts at and away from the parent's face during the FFSF. IJA was calculated as a mean frequency during the Early Social Communication Scales (ESCS) at 8, 10, 12, 15, and 18 months. A mean of receptive and expressive language abilities at 24 and 36 months was calculated using the Mullen Scales of Early Development. Later ASD symptomatology was measured as the sum of the Communication and Social Interaction Total and the Stereotyped Behaviors and Repeated Interests Scales of the Autism Diagnostic Observation Schedule (ADOS) at 30 months.

Results:

Overall, there were strong associations in ASD-sibs between early gaze shifts and IJA, and between IJA and ASD symptomatology. Gaze shifts were significantly correlated with IJA for ASD-sibs, $r(24) = .49$, $p = .02$, but not for COMP-sibs, $r(18) = .21$, $p = .40$. In addition, IJA was significantly correlated with ASD symptomatology for ASD-sibs, $r(8) = -.77$, $p = .03$, but not for COMP-sibs, $r(10) = -.39$, $p = .26$. There was some degree of negative association between gaze shifts and ASD symptomatology for ASD-sibs, $r(8) = -.64$, $p = .09$, but not for COMP-sibs, $r(10) = .21$, $p = .56$. Both ASD and COMP-sibs exhibited similar associations between IJA and later language. There was a tendency for IJA to be associated with receptive language for ASD-sibs, $r(15) = .48$, $p = .07$, and that correlation was significant for COMP-sibs, $r(12) = .59$, $p = .04$.

There was a tendency for IJA and expressive language to be associated for ASD-sibs, $r(15) = .49$, $p = .07$, and COMP-sibs, $r(12) = .55$, $p = .06$. Gaze shifts were not correlated with later language.

Conclusions:

Among ASD-sibs, flexible attention allocation at and away from the parent's face at six months was associated with language and ADOS symptomatology two years later. In addition, in ASD-sibs, greater frequency of gaze shifts at six months predicted more frequent IJA behaviors from 8 to 18 months, which in turn predicted lower ASD symptomatology at 30 months. COMP-sibs did not exhibit developmental associations between visual and joint attention, and later ASD symptomatology. For ASD-sibs, early deficits in visual and joint attention may predict atypical developmental and later ASD symptomatology.

105.86 86 Atypical Face Scanning in Unaffected High-Risk Infant Siblings. K. Chawarska*, F. Shic, J. Bradshaw, S. Macari and A. Klin, *Yale University School of Medicine*

Background:

Toddlers with Autism Spectrum Disorder (ASD) exhibit an atypical distribution of attention when examining faces. It is not clear, however, when these abnormalities first manifest, and whether these attentional alterations are shared by unaffected first-degree relatives.

Objectives:

To examine developmental changes in the scanning of static, dynamic, and speaking faces in the first year of life in low-risk typically developing (TD) infants (N=24) and in infants who, due to genetic liability, are at high-risk for ASD (N=31). The latter group was further subdivided based on 18-month assessment into those who developed symptoms of autism spectrum disorder (ASD, N=5) and those who appeared unaffected (NAF, N=26). An additional group of infants with questionable phenotype at 12 or 18 months were excluded from this analysis.

Methods:

Infants were tested at 3, 6, 9, and 12 months. Each infant viewed three types of faces: Static, Dynamic, and Speaking. Responses were recorded with an eyetracker. Average percentages of time spent monitoring specified face regions were examined as a function of age, group, and display. ASD infant comparisons were qualitative due to small N.

Results:

Attention to faces in general and to their internal features (eyes, nose, and mouth) increased rapidly from 3 to 6 months in TD and NAF groups. Regardless of age, infants primarily monitored the eyes in the Static condition, less in the Dynamic condition, and least during Speech. The pattern was reversed for the mouth region, that was primarily attended to during Speech and least during the Static condition. Specifically for mouth viewing, age differentially affected attention between groups. In TD infants, it increased rapidly between 3 and 9 months, likely reflecting reliance on visual cues in encoding speech sounds. Between 9 and 12 months attention to the mouth dropped significantly in TD group possibly due to a lesser reliance on lip-reading in speech perception. However, in NAF infants, attention to mouth continued to increase from 3 to 12 months. NAF infants also spent more time examining outer facial features than TD controls. In comparison, responses of infants with ASD were variable and different from NAF and TD infants, with differences becoming particularly apparent at 9 months in the condition involving infant-directed speech.

Conclusions:

TD and NAF infants modulate their scanning strategies depending on the context in which faces are presented. Amount of attention directed to the mouth varies by age, most likely due to its role in speech perception. Though, unaffected high-risk infants exhibit a less mature strategy reflected in more time spent examining the outer regions of the face. At 12 months they spent more time examining the mouth than TD controls, suggesting that they might still rely on visual processing of articulatory movements for sound discrimination. These findings suggest that even apparently symptom-free infants show mildly atypical face scanning patterns associated with their genetic risk status possibly linked to purported vulnerabilities in language development. Considering high variability amongst symptomatic infants, their results will be discussed individually in a context of symptom severity and levels of developmental skills.

105.87 87 Characterization of the Broader Autism Phenotype in Later-Born Siblings. E. E. Malesa* and W. Stone, *Vanderbilt University*

Background: Research has found that some family members of children with autism spectrum disorders (ASD) exhibit qualitatively similar, yet milder features of ASD described as the "Broader Autism Phenotype" (BAP). Few have characterized this group from a developmental standpoint, by comparing characteristics of BAP in young siblings of children with ASD (Sibs-ASD) to children with ASD and typical development (TD) at different points in development. BAP subgroups appear to exhibit similar levels of ability in autism related symptomatology such as responding to joint attention (RJA; Sullivan et al., 2006) and language (Gamliel et al., 2007) at 14 months. However, when reassessed (at 24 and 54 months, respectively), these BAP subgroups demonstrate significant developmental gains, showing profiles more similar to TD children.

Objectives: The purpose of the current study was to broaden our understanding of early manifestations of BAP in Sibs-ASD by comparing their performance to Sibs-ASD with ASD outcomes and later-born siblings of TD children (Sibs-TD) on a variety of developmental domains related to autism symptomatology.

Methods: *Participants*: Forty-nine (49) Sibs-ASD and 30 Sibs-TD participated. Children were initially seen at 12-23 months and were reassessed 17-23 months later (mean CAs=15 mos and 34 mos, respectively). At T2, 6 Sibs-ASD (12%) were diagnosed with ASD (3 PDD-NOS; 3 Autistic Disorder) and 8 (16%) were classified as BAP according to two *a priori* criteria: ADOS social algorithm score exceeding cutoff, and clinician concern about the child's social development. No Sibs-TD received a diagnosis. *Measures*: Autism severity was assessed using the Childhood Autism Rating Scale (CARS), cognitive abilities were assessed using the Mullen, and social-communication skills were assessed using measures of initiating joint attention (IJA), RJA, and the Social Behavior Checklist (SBC).

Results: At T1, siblings later classified as BAP did not differ from those with ASD in any of the domains assessed, but showed significantly lower abilities than Sibs-TD in social-communicative skills (IJA, $t(36)=-2.89$, $p=.006$; RJA, $t(36)=-4.88$, $p<.001$) and cognitive development (Visual Reception, $t(36)=-2.04$, $p=.049$). At T2, children with BAP differed significantly from those with ASD by showing less autism symptomatology (CARS, $t(12)=-2.58$, $p=.024$), higher social-communicative skills (IJA, $t(12)=4.82$, $p<.001$; RJA, $t(10)=2.70$, $p=.022$), and higher cognitive skills (Fine Motor, $t(12)=2.28$, $p=.041$; Receptive Language, $t(12)=3.38$, $p=.005$; Expressive Language, $t(12)=4.67$, $p=.001$; ELC, $t(12)=3.30$, $p=.006$). Relative to Sibs-TD, those with BAP at T2 demonstrated significantly more autism symptomatology (CARS, $t(36)=4.21$, $p=.003$), lower social-communicative skills (RJA, $t(34)=-2.72$, $p=.010$; SBC, $t(33)=-4.75$, $p<.001$) and lower overall cognitive ability (ELC, $t(36)=-2.06$, $p=.047$).

Conclusions: These results replicate and extend those previously reported. In the second year of life, siblings later classified as BAP differed from Sib-TD controls in several developmental domains, but did not differ from siblings with ASD outcomes. When reassessed 18 months later, the BAP group showed weaker performance than the Sib-TD group, and also differed from the ASD group in all domains. These results suggest a developmental growth trajectory in the BAP group that exceeds that of the ASD group. Continued follow-up and replication with larger samples is needed to understand the implications of these findings.

105.88 88 Impairment in Empathic Response Is Evident by 12 Months of Age in Children Subsequently Diagnosed with ASD. J. Barnwell*[1], T. Hutman[2], A. D. DeLaurentis[2], A. Rozga[3], C. Sugar[2] and M. Sigman[2], (1)*University of North Carolina at Chapel Hill*, (2)*University of California, Los Angeles*, (3)*Georgia State University*

Background: Empathic response is impaired in preschool-age and older children with autism (Sigman, Kasari, Kwon & Yirmiya, 1992; Yirmiya, Kasari, Sigman & Mundy, 1992). However, little is known about the development of empathy in infants who are subsequently diagnosed with autism, relative to infants who develop typically. Objectives: To examine empathic response at 12, 18, and 24 months among siblings of children with autism who subsequently received an autism diagnosis (ASD), siblings who developed typically (high-risk TD), and typically developing control group infants (low-risk TD). We examined the developmental trajectory of empathic responsiveness in the three groups and explored links with language skills.

Methods: Participants included 103 infant siblings of children with autism and 55 infants with no family history of autism. 14 children in the high-risk group developed an ASD by 36 months, as determined by the ADOS and clinicians' judgment. Children's reactions to an examiner's display of pain were evaluated at 12, 18, and 24 months and coded for interest and concern using four-point Likert scales.
Results:
Empathy scores (0-3) were cross-tabulated with group membership (ASD, high-risk TD, low-risk TD) for both the interest and concern scales. Chi-square analyses confirmed an association between group and empathic response scores for both scales at all 3 time points (all ps < 0.01).
For the second set of analyses, empathy scales were collapsed to form dichotomous variables. Ratings of 0 or 1 were classified as low interest or low concern; ratings of 2 and 3 were classified high interest or high concern. Score patterns across time-points were cross-tabulated with group membership. An association between group and pattern was detected for interest ($\chi 2(14) = 61.90$, $p < .0001$), but not for concern. Infants who developed an ASD tended to show lower interest scores and little improvement, whereas both high- and low-risk TD groups showed improvement or they had high scores across all three time points.
Predictors of achieving higher levels of interest and concern were examined using logistical regression analysis. Group membership predicted achievement of high interest ($p = .0007$) and high concern ($p = .0009$), even when verbal ability was included in the model. Both TD groups performed significantly better than the ASD group. Age was not a significant predictor of empathic response.
Conclusions: Impaired empathic response, indicated by decreased level of interest and concern with respect to an examiner's display of pain, is evident by the age of twelve months in children who are subsequently diagnosed with an ASD. Differences in developmental trajectory of empathic response are in evidence at least through the second birthday, with infants diagnosed with ASD failing to show improvement in empathic response over time.
Funding: NIH/NIMH Studies to Advance Autism Research and Treatment (STAART) Grant# U54-MH-068172 (Marian Sigman, P.I.)

105.89 89 Diagnostic Stability of Autism Spectrum Disorder Diagnoses Made Before Age Two. C. Chlebowski*, M. Barton, S. Hodgson and D. Fein, *University of Connecticut*

Background: Research suggests that a diagnosis of Autistic Disorder (AD) is valid and stable when made at age two (Kleinman et al. 2007; Lord, 1995; Stone et al., 1999). However, less is known about the diagnostic stability of AD and PDD-NOS diagnoses made prior to age 2.
Objectives: To examine the diagnostic stability for Autistic Disorder and PDD-NOS diagnoses made before age 2.
Methods: Participants were 41 children who were screened with the M-CHAT (Robins, et al., 2001), and were evaluated and diagnosed with an autism spectrum disorder before age 2 (mean age at diagnosis=21 months). All children were reevaluated at age 4 (mean age=49 months) and diagnostic stability across the two time points was assessed.
Results: Of the 24 children who were diagnosed with Autistic Disorder before age 2, 83% (n=20) retained the diagnosis at age 4; 8% (n=2) received a PDD-NOS diagnosis at reevaluation; and 8% (n=2) moved off the spectrum. Of the 17 children diagnosed with PDD-NOS before age 2, 47% (n=8) retained the diagnosis, 24% (n=4) received a diagnosis of Autistic Disorder, and 29% (n=5) moved off the spectrum.
Conclusions: Results indicate that a diagnosis of Autistic Disorder has strong diagnostic stability even when diagnosed before age 2, though a diagnosis of PDD-NOS is less stable, with approximately 50% of children losing the diagnosis of PDD-NOS at reevaluation.

105.90 90 Does 24-Month Empathic Responding Predict Autistic Symptomatology and Later ASD Diagnosis?. N. M. McDonald*, G. Robinson and D. S. Messinger, *University of Miami*

Background: There is evidence that individuals with Autism Spectrum Disorders (ASDs) have deficits in recognizing and responding to other's emotional experiences. In typically developing individuals, the ability to connect with other's emotions, or empathize, is associated with increased social competence. Consequently, it may be that a disturbance in the ability to empathize in people with ASDs contributes to the social and communication deficits that define the disorder. Despite the potential relevance of empathy deficits, little is known about how early empathic responding relates to autistic symptomatology and eventual diagnosis. The current study used a prospective method to investigate early empathic responding in younger siblings of children with an ASD, who are at

increased genetic risk for the disorder, and children with typically developing older siblings.

Objectives: To investigate whether early empathic responding predicts later autistic symptomatology and ASD diagnosis.

Methods: Children at varying risk for an ASD were measured for empathic responding at 24 months and autistic symptomatology at 30 and 36 months. Empathic responding was measured from children's responses to parental distress during a free play session. Children were given an overall Empathy rating from 1 to 7. Autistic symptomatology was measured with the Autism Diagnostic Observation Schedule (ADOS) and the Autism Diagnostic Interview (ADI). Participants were later diagnosed by an independent clinician, according to DSM-IV criteria, as having Autistic Disorder (AD), Pervasive Developmental Disorder – Not Otherwise Specified (PDD), or No ASD.

Results: Preliminary analyses were conducted with 24-month Empathy rating and 30-month ADOS score. Empathy rating at 24 months predicted 30-month ADOS score, $F(1,24)=5.13, p<.05$, explaining 18% of the variance, so that children displaying less early empathic responding showed more autistic symptomatology on the ADOS. Preliminary analyses were also conducted with 24-month Empathy and eventual diagnosis. For this analysis, AD and PDD diagnoses were collapsed into one ASD group and compared to the No ASD group. The children later diagnosed with an ASD ($M=1.90$, $SD=0.99$, $n=10$) had lower 24-month Empathy ratings than the No ASD group ($M=3.60$, $SD=1.58$, $n=10$), $F(1,18)=8.31, p=.01$. A linear regression analysis with 24-month Empathy and 36-month ADI score will also be conducted.

Conclusions: This is the first study to look prospectively at early empathy development in children with ASDs. Results of preliminary analyses demonstrate that children who are later diagnosed with an ASD display less empathic responding than children with no ASD at 24 months of age, and that 24-month empathic responding predicts later ASD symptomatology, as measured by the ADOS. These results suggest that empathic responding around two years of age may be an important marker for future ASD diagnosis. Further analyses will be conducted as sample size increases.

105.91 91 Defining Social Engagement Deficits in Young Children with ASD: Similarities Between Retrospective and Prospective Parental Reports. E. B. Lee* and W. Stone, *Vanderbilt University*

Background: Social-communicative impairments are essential features of autism spectrum disorders (ASD) and are thought to appear before three years of age. However, methodological challenges have hampered investigations into the nature of these early deficits, particularly in infants/toddlers who may not receive diagnoses until the preschool years. Moreover, social engagement in young children with ASD is typically not absent, as social behaviors may be present but qualitatively different from those seen in typically-developing peers. Measures such as the Detection of Autism by Infant Sociability Interview (DAISI) (Wimpory et al., 2000) show promise in identifying deficits in social engagement associated with ASD that may aid in early identification and intervention.

Objectives: To identify specific social engagement deficits in young children with and at risk for ASD.

Methods: *Measure:* Social engagement was measured using the Detection of Autism by Infant Sociability Interview (DAISI) which is a 19-item parental interview assessing social behaviors typically occurring within the first 24 months of life. Each behavior is scored as present or absent. The DAISI was used with two samples to identify the most robust behaviors differentiating children from ASD from other comparison groups. *Samples:* Sample 1 comprised 31 children with ASD (23 autism, 8 PDD-NOS) individually matched on CA and MA to 31 children with Developmental Delay (DD) (mean CAs = 34 months and 33 months, respectively). Parents were interviewed about their child's **past** behavior in the first 2 years during a research evaluation. Sample 2 comprised 49 later-born siblings of children with autism (Sibs-ASD) (mean CA = 15 months) participating in a longitudinal follow-up study. For this sample, parents were interviewed about their child's **current** behavior. Results for children with a follow-up diagnosis of ASD (n=6) or Broader Autism Phenotype (BAP; n=8) were compared with those who received no diagnosis at follow-up (n=35) (mean CA = 34 months).

Results: For Sample 1, ASD-DD comparisons revealed significant differences in the proportion

of parents endorsing 9 DAISI items: frequency and use of eye contact, giving and showing objects, pointing and following a point, teasing, and preverbal turn-taking and communication (all ps < .05). Seven of the 9 behaviors were identical to those differentiating ASD and DD groups in the original study (Wimpory et al., 2000). For Sample 2 (Sib-ASD), significant group differences for 4 items (i.e., use of eye contact, showing, pointing, and waving) were found between the siblings who later received an ASD or BAP diagnosis and those with no diagnosis. In both samples, differentiating items received a lower percentage of positive responses in the autism-related group.

Conclusions: In both retrospective and prospective samples, young children with - or at risk for - ASD showed a distinct pattern of social engagement relative to nonautistic samples. This study replicates and extends Wimpory et al.'s (2000) findings with a larger sample and demonstrates the potential utility of the DAISI for early identification of ASD in young, high risk samples.

105.92 92 Oculomotor Behavior in Toddlers with Autism during Naturalistic Viewing of Social Scenes. C. J. Zampella*, W. Jones and A. Klin, *Yale University School of Medicine*

Background: Previous research has investigated properties of visual saccades and fixations in school-aged children with autism spectrum disorders (ASD) using a natural viewing paradigm. The results confirm findings from two separate bodies of literature, indicating that basic mechanisms of oculomotor function are intact in children with ASD, but that children with ASD differ from their typically-developing peers in terms of the social content on which they preferentially focus. Other research has studied viewing patterns in two-year-olds with ASD during naturalistic viewing and has found that toddlers with ASD also exhibit a preference for different aspects of a social scene than typically-developing toddlers and toddlers with non-autistic developmental delays. However, investigation into the ability to control eye movements during a natural viewing task has not yet been extended to these very young children with ASD. The current study intends to address that topic.

Objectives: To compare oculomotor properties of visual fixations and saccades during naturalistic viewing of social scenes in toddlers with ASD, typically-developing toddlers and toddlers with non-autistic developmental delays.

Methods: Eye-tracking data were collected while toddlers watched film clips of actresses playing the role of caregiver. From these data, fixations and saccades were identified. Data on the frequency and duration of fixations, and on the frequency, duration, velocity, and amplitude of saccades, were then compared across groups.

Results: Preliminary analyses suggest that basic properties of saccades and fixations do not differ between two-year-olds with ASD, typically-developing controls and controls with non-autistic developmental delays.

Conclusions: Basic oculomotor circuitry appears to develop normally in individuals with ASD by two years of age. This suggests that discrepancies in viewing patterns between toddlers with ASD and their typically-developing and developmentally-delayed peers are not the result of oculomotor impairments, but rather reflect differences in what aspects of a social scene are most salient to them.

105.93 93 Ecobehavioral Assessment of Social Behaviors of Young Children with Autism across Treatment Models. A. M. Sam*[1], B. P. Humphreys[1], S. McDonough[2] and K. Hume[1], (1)*Frank Porter Graham Child Development Institute, University of North Carolina, Chapel Hill*, (2)*University of North Carolina*

Background: Children with autism participate in a variety of early childhood settings such as inclusive classrooms with typical peers, self-contained classrooms for children with autism only, and classrooms serving children with non-specific developmental disabilities. However, the comprehensive treatment models associated with these varying classroom compositions for children with autism have a limited evidence base of support. An important starting place in establishing an evidence base would be to understand how different treatment models and their associated perspectives on classroom composition affect the core deficit area of social interaction. The National Research Council (2001) identified a need for comparative studies on the social outcomes of young children with Autism Spectrum Disorder (ASD) served in different comprehensive treatment programs. Ecobehavioral assessment, which involves direct observation of classroom ecology and teacher-child behavior, was used to evaluate the social behaviors of young children with ASD across three treatment models. Objectives: (1) To examine the social behaviors of young children with ASD across three comprehensive intervention models

that use different classroom compositions. (2) To describe the class ecology (i.e. structural features) for students served in these TEACCH (ASD only), LEAP (inclusive), and control classrooms (children with a range of disabilities) (termed Business as Usual or BAU). Methods: Participants included 67 preschool age children with ASD located in 3 states. Thirty children were enrolled in 9 TEACCH classrooms, 19 children in 6 BAU classrooms, and 16 children in 9 LEAP classrooms. Research staff collected 30-minute observational samples for each student. An ecobehavioral coding system, the Code for Active Student Participation and Engagement (CASPER), was used to assess the structural features of the classroom and child behaviors. Momentary time sampling was used to code the following variables at 10-second intervals: group arrangement, class activity, activity initiator, child behavior, child social behavior, and adult behavior. Results: Data analysis is ongoing, however, preliminary results indicate that social behavior occurred in less than 6% of intervals across the three treatment models (5.4% TEACCH/AU only, 5.2% BAU/developmental delay, 4.4% LEAP/inclusive). In TEACCH and BAU classrooms, over 80% of social behavior was directed towards adults, while in LEAP classrooms, social behavior was directed equally to both adults and peers. Students in LEAP classrooms were most likely to be social in small groups with peers (88%) during socio-dramatic play activities. In TEACCH classrooms students with ASD primarily engaged socially during 1:1 activities with adults (59%), typically while working on sensory/pre-academic skills. In BAU classrooms, students were most likely to engage socially during 1:1 activities (46%) during manipulative play. ANOVAs will be reported to examine group differences. Conclusions: These early findings indicate that across intervention model and class composition, children with ASD rarely engaged in social behavior. However, the ecological variables that facilitated social engagement did differ across the model types. In addition, the recipients of the child's social behavior (peer or adult) also differed. Further analysis will assist in describing and differentiating the social behavior of children across model type and defining ecological variables that are related to social behavior.

105.94 94 Impaired Face but Not Object Recognition in Young Children with Autism Spectrum Disorders. J. Bradshaw*, F. Shic and K. Chawarska, *Yale University School of Medicine*

Background: Social impairments are inherent in individuals with Autism Spectrum Disorders (ASD), making the processing of social stimuli a primary area of research. Face recognition specifically has been found to be atypical in older children and adults with ASD. Recently we documented that both scanning and face recognition is atypical in young children with ASD as well. However, it is not clear if deficits in recognition are restricted to faces or represent a generalized deficit in fast and implicit processing of novel stimuli, regardless of their social content.

Objectives: This study examined whether difficulties in recognition observed in young children with ASD are limited to faces or whether they reflect a global impairment of recognizing novel stimuli, including those void of social information.

Methods: Fifteen toddlers with ASD (age:M=41.5m,SD=14) and fifteen typically developing (TD) controls (age:M=38.2m,SD=7) were included in this study. All children underwent cognitive and diagnostic testing to confirm appropriate group placement. Each child was tested in a Visual Paired Comparison (VPC) paradigm, an approach used for studying visual stimulus processing that assumes an individual will fixate longer on a novel stimulus than on a paired familiar stimulus. This novelty preference (NP) is operationalized as successful processing and recognition, and is calculated as the ratio of looking time at the novel stimulus to looking time at both the novel and familiar stimulus. Every child was shown twelve VPC trials split into two conditions: Objects and Faces. Each trial included a recognition and a familiarization phase. During familiarization, a photograph of either an object or face was presented on the screen. A gray screen then appeared for five seconds followed by the recognition phase where the familiar image was displayed next to a comparable, novel image. Visual responses were recorded using an eye tracker.

Results: Duration of looking at the stimulus during familiarization did not differ between groups. In the Objects condition, there was no significant difference in the NP between the ASD and TD groups, and both had a NP significantly above chance, suggesting that both groups successfully encoded and recognized the objects (ASD:M=.56(.11),t(14)=2.26,p<.05;

TD:M=.58(.09),t(14)=3.56,p<.01). However in the Face condition, a significant difference emerged in the NP between groups (ASD:M=.52(.11); TD:M=.59(.07),p<.05). The TD group had a NP that was significantly above chance (t(14)=4.85,p<.001), while the ASD group showed no preference for the familiar or novel face (t(14)=.619).

Conclusions: Results of the study indicate that in young children with ASD, visual recognition deficits in faces do not extend to objects. Both groups demonstrated a preference for the novel objects, implying that children with autism are not impaired in encoding and recognizing a complex but nonsocial stimulus. However when viewing faces, children with ASD showed no novelty preference, as compared to their TD peers who were able to recognize the familiar face. Although children with autism spend as much time looking at a face as TD children they are not encoding and processing in the same manner, which could have implications for development of social interaction skills.

105.95 95 Language and Cognitive Profiles in Young Children with Autism: Gender Differences. A. M. Mastergeorge[1], S. J. Rogers[1], S. Ozonoff[2], L. Cochran*[1], L. Deprey[3] and P. Shoja[1], (1)*M.I.N.D. Institute, University of California at Davis*, (2)*M.I.N.D. Institute, University of California at Davis Medical Center*, (3)*UC Davis Medical Center*

Background: Language deficits and delays are a hallmark of young children diagnosed with autism spectrum disorders. Differences in the incidence of autism by gender is well documented; however there is scant information regarding the pattern of language skills and gender profiles in young children with autism. Understanding the profiles of young children with autism can inform developmental trajectories and provide salient evidence for treatment approaches.,Objectives: The purpose of this study is to examine the language and cognitive profiles with autism spectrum disorders to further our understanding of autism phenotypes and subtypes of autism in the context of language skills.,Methods: Participants included 24 children diagnosed with ASD (12 boy and 12 girls) with ages ranging from 24-42 months who were also matched on age and developmental level. Children were classified as verbal or nonverbal based on the Autism Diagnostic Observation Schedule, and assessed using the Mullen Scales of Early Learning, the Expressive One Word Picture Vocabulary Test, the Peabody Picture Vocabulary Test, and language subtests of the Vineland Adaptive Behavior Scales.,Results: The results indicated that the young girls with autism demonstrated significant deficits on all language and cognitive profiles when compared with the young boys with autism on both verbal and nonverbal measures of cognition, and language (both receptive and expressive measures). A previous study conducted by Lord, Schopler & Revicki, (1982) reported males showing more advanced skills on the PPVT and nonverbal IQ in children ages 3 to 8 year olds; however the receptive skill differences disappeared when nonverbal IQ was controlled. Other studies examining gender have been with older children and adults, and have not examined profiles in very young children with autism. Conclusions: The preliminary results of the current study may indicate neurocognitive mechanisms underlying language processing in young children with autism that have both theoretical and clinical implications. While language skills may be independent of IQ in autism, it is clear that it is important to understand developmental profiles that may have long term prognostic indicators for young children with autism, and the influence that sex differences may play in the domain of language skill development.

105.96 96 Bodily and Procedural Imitation in Preschoolers at Risk for Autism. M. Vanvuchelen*[1], H. Roeyers[2] and W. De Weerdt[3], (1)*Katholieke Universiteit Leuven - University College of the Province of Limburg, Belgium*, (2)*Ghent University*, (3)*Katholieke Universiteit Leuven*

Background:
The insight in the nature of imitation problems in autism has evolved rapidly.
However, the query if these problems are general or specific remains subject of debate.

Objectives:
Present study sought to examine bodily and procedural imitation in preschoolers at risk for autism, using a standardised imitation test.

Methods:
Participants:
85 children, aged 1.9-4.5 years, taught to be autistic, and consecutively referred to University Autism Clinics in Flanders (Belgium).
A multidisciplinary clinical consensus classification (DSM-IV-TR) revealed: 68 children with Autism Spectrum Disorder (ASD) and 17 with Non-Spectrum Developmental Disorder (NS-DD).

Instrument:
Preschool Imitation and Praxis Scale (PIPS) (Vanvuchelen, Roeyers, De Weerdt).
Bodily and procedural imitation age-equivalent scores were derived from PIPS scores of 654 healthy children (1y-4.9y).
Differences between imitation age-equivalent scores and non-verbal mental age were used as criteria for imitation delays.

Results:
In children with ASD, both bodily ($z=-4.0$, $p<0.01$) and procedural ($z=-2.1$, $p=0.03$) imitation ages were significantly below the non-verbal mental age.
In contrast, in children with NS-DD, bodily ($z=-1.2$, $p=0.21$) and procedural ($z=-1.4$, $p=0.13$) imitation ages were not significantly different from the non-verbal mental age.

Conclusions:
Differences between bodily, respectively procedural imitation ages and non-verbal mental age can serve as criteria for imitation delays. Findings suggest general imitation problems, i.e. bodily and procedural, in children with autism spectrum disorders.

References:
Vanvuchelen, Roeyers, De Weerdt, (2008) The Preschool Imitation and Praxis Scale (PIPS). Development, Reliability and Factor structure. *Submitted to Psychological Assessment*.

105.97 97 Face/Object Perception in Infant Siblings of Children with Autism Spectrum Disorders (ASD). K. Dobkins*, L. Carver and V. Sampath, *University of California, San Diego*

Background: Previous behavioral and neural studies have revealed face processing atypicalities in individuals with Autism Spectrum Disorders (ASD) and their first-degree relatives. Because these atypicalities are seen in both affected and unaffected family members, they may be considered an "endophenotype" of ASD, reflecting a genetically-mediated risk factor for the disorder. Objectives: To study the development of this potential endophenotypic marker, we investigated Face vs. Object perception in 8-month-old infant siblings of children with ASD ("High-Risk" infants) in comparison to infants from families without autism history ("Low-Risk" infants), using stimuli identical to those employed in our event-related potentials (ERP) study measuring neural responses to Faces vs. Objects at 10 months of age. Methods: Forced-Choice Preferential Looking was used to measure infants' preferences in three different Face/Object studies: 1) "Faces vs. Objects": This measured infants' preferences for pictures of Faces vs. Objects (the objects being Toys), with values greater than 50% indicating a significant face preference. 2) "Faces vs. Objects: Inversion Effects": This study compared infants' preferences for Upright vs. Inverted Faces to their preferences for Upright vs. Inverted Objects (the objects being Strollers), with "Difference Scores" [Upright Pref(faces)-Upright Pref(objects)] greater than 0% indicating a greater inversion effect for Faces. 3) "Emotional Faces": This measured infants' preferences for different emotional valences (Happy vs. Disgusted vs. Neutral), with values greater than 50% indicating a preference for one emotion over another. Pictures of Faces and Objects were manipulated in Matlab so that they were matched in luminance, contrast and spatial frequency content. Results: In Study 1, both subject groups showed a significant preference for Faces over Objects, although the effect was larger in Low-Risk (67%) than High-Risk (60%) infants. In Study 2, both subject groups exhibited a significantly larger inversion effect for Faces than for Objects (Difference Score ~12%), with no difference between groups. Preliminary data from Study 3 suggest that while Low-Risk infants preferred Disgusted over Neutral Faces, High-Risk infants exhibited the opposite preference. Conclusions: These preliminary behavioral data suggest differences in Face/Object perception between High-Risk and Low-Risk infants, although group differences appear smaller than those observed in our ERP measures. Together, our behavioral and ERP measures of Face/Object processing provide a potential endophenotypic marker associated with ASD.

105.98 98 Correlates of Elicited and Spontaneous Imitation in Young Children with Autism. K. Meyer* and B. Ingersoll, *Michigan State University*

Background: Children with autism have been found to be significantly impaired in imitation skills. Previous research on imitation in autism has focused primarily on different forms (e.g., object vs. gesture) and different time courses (immediate vs. deferred) of imitation, suggesting that children with autism are more impaired in some imitative areas than others and that some aspects of imitation are more closely associated

with other social-communication skills than others. Recently, there has been an interest in examining different contexts of imitation. McDuffie et al. (2007) demonstrated that elicited imitation is associated with ability to follow another's attention, whereas spontaneous imitation is associated with social reciprocity, suggesting that imitation in different contexts may be mediated by different underlying skill sets.

Objectives: The goal of this study is to replicate McDuffie et al.'s findings regarding different predictors of imitation performance in elicited and spontaneous contexts, and to examine whether elicited and spontaneous imitation differ in their relationship with other social-communication skills.

Methods: Twenty-three children with autism between the ages of two and four were administered standardized assessments of their cognitive, language, play, joint attention, social reciprocity, and elicited and spontaneous imitation skills.

Results: After controlling for developmental level, spontaneous, but not elicited, imitation skills were associated with social reciprocity, replicated previous findings by McDuffie et al. (2007). Both elicited and spontaneous imitation skills were associated with symbolic play.

Conclusions: Elicited and spontaneous imitation skills likely represent different skills sets, with the ability to imitate spontaneously being more closely associated with social interest than the ability to imitate in response to direction. However, both types of imitation seem to play a role in the development of symbolic play.

105.99 99 The Development of Imitation Abilities in Children with Autism. G. Vivanti*[1], S. Hepburn[2], A. Philofsky[3] and S. J. Rogers[4], (1)*M.I.N.D. Institute, University of California at Davis Medical Center*, (2)*University of Colorado Denver School of Medicine*, (3)*University of Colorado at Denver*, (4)*M.I.N.D. Institute, University of California at Davis*

Background: The research on imitation in autism over the last 30 years has consistently reported impaired imitative abilities in children with ASD at all ages. However, little is known about the developmental course of imitation skills in ASD

Objectives: The aim of the study is:
1) to analyze the developmental profile of imitation skills in children with autism by examining their imitation abilities at three different ages (3, 5, and 8)
2) to analyze group differences in imitation abilities between children with autism and children without autism at three different ages
3) to determine the contribution of skills in social and cognitive development in children with and without autism
4) to determine the contribution of early social and cognitive skills in the development of imitation abilities in children with and without autism

Methods: A cohort of 27 children with autism, 35 children with a developmental disability and 20 typically developing subjects matched for age were tested on a series of imitation tasks when they were 3 (Time 1), 5 (Time 2) and 8 years old (Time 3). Measures of social, cognitive and motor skills were also collected at all ages.

Results: At Time 1 children with autism imitate less accurately than typically developing children and children with developmental disabilities. Preliminary analyses on a subgroup of participants suggest that over the time all groups show significant improvements, however at Time 3 children with autism are still less accurate than typically developing children in imitating. Analyses on the developmental disability group are in progress. Across the entire sample imitation performances at different Time points are highly correlated even when group appartenence is controlled for. In the autism group, severity of symptoms, cognitive, verbal and motor skills at Time 1 are associated to difficulties in imitation at Time 1 and 2 .

Conclusions: Children with autism show difficulties imitating others at age 3. Their abilities improve over time but are still deficient 5 years after the first assessment. In progress analyses will analyze what factors are related to both group and individual differences

105.100 100 Spatial Incongruity Affects the Looking Behavior of Children with High Functioning Autism during Joint Attention Eliciting Videos: An Eye Tracking Study. M. Jaime*[1], B. Gamber[1], C. Hileman[1], L. C. Newell[2], H. A. Henderson[1] and P. C. Mundy[3], (1)*University of Miami*, (2)*Indiana University of Pennsylvania*, (3)*UC Davis*

Background: Joint attention involves following the gaze of another with an expectation to see an object or event. However, little is known about how looking behavior is affected by incongruent spatial cues during joint attention. Moreover,

does spatial incongruity differentially affect the looking behavior of children with autism?

Objectives: In this study we used eye-tracking technology to examine looking behavior under both congruent and incongruent joint attention conditions in a sample of high functioning children with autism and a typically-developing comparison group.

Methods: Thirty children ranging in age from 10-18 years (M = 14.47, SD = 2.72) participated in the study. Seventeen had a diagnosis of high functioning autism (HFA) and 13 were typically developing (TD). Participants watched a series of 12 joint attention eliciting videos (29 s in duration each) of a male looking towards a dot appearing in one of the four corners of the screen (Williams et al., 2005). They were instructed to "follow the dot" as they watched the videos. During congruent videos, the direction of gaze matched the area in which the dot appeared. For the incongruent videos, the direction of gaze did not match the location of the dot. The order of presentation of videos was randomized across participants. A Tobii x50 eye-tracker was used to obtain participants' looking behavior. Areas of interest were drawn using the Clearview 2.7.1 software and consisted of a "face" area and a "gazed-at" area. Proportion of total looking (PTL) to either the face or gazed-at area was calculated by dividing the total duration of looking (in ms) to either the face or gazed-at area by the total duration of looking at the videos.

Results: Preliminary results revealed that children in both groups spent a significantly greater PTL to the face rather than the gazed-at area. However, this result was qualified by interactions with (a) diagnostic group, and (b) the congruency of the stimuli. Specifically, the HFA group showed a marginally greater PTL to the face area relative to participants in the comparison group, F (1, 31) = 4.03, p = .054; however, diagnostic group was unrelated to PTL to the gazed area. In addition, both groups, showed a significantly greater PTL to the face relative to the gazed-at area during incongruent videos, F (1, 31) = 51.208, p < .001, whereas during congruent videos looking was more equally distributed between the face and gazed areas.

Conclusions: These results demonstrate that for all individuals, looking to the face increases during incongruent gaze processing suggesting that individuals may be searching for additional social information. This pattern of increased looking to the face, rather than the direction of gaze, was exhibited by HFA participants across all trial types, suggesting a more effortful processing of social information during joint attention.

105.101 101 Visual Processing of Hierarchical Stimuli in Typically Developing Infants. J. Gibson[1], A. Needham[1], J. T. Elison*[2] and J. S. Reznick[2], (1)*Duke University*, (2)*University of North Carolina at Chapel Hill*

Background: Research suggests that individuals with autism may process visual stimuli differently than their typically developing peers. Previous work has shown that children and adults with autism show a bias for detail-oriented processing; however, typical adults demonstrate a global bias when performing hierarchical tasks. Similarly, research suggests that infant siblings of children with autism show abnormalities in tasks that elicit visual processing in the magnocellular pathway, which carries global aspects of information such as contrast sensitivity and coarse spatial information. Despite evidence of processing differences between autistic and typical adults, little is known about the developmental trajectory of global versus local biases in perceptual processing in infants or young children. Understanding how a global bias develops in typically developing children could offer insight into the processing differences seen between autistic and typical individuals.

Objectives: This study was designed to determine the developmental trajectory of visual processing biases during the first year of life in typically developing infants in order to generate data that could inform future studies of infants at risk for developing autism.

Methods: Participants were healthy infants (gestational age ≥ 37 weeks at birth) aged three and four months (N=7, mean age = 15.5 weeks), six and seven months (N=12, mean age = 30.8 weeks), and twelve and thirteen months (N=14, mean age = 57.0 weeks). The infants watched a 110-second presentation on a 17" computer monitor. During six 15-second familiarization trials, the infant viewed a large letter ("E" or "H") made of smaller letters ("E" or "H", whichever was not the global element). The infant was then given a forced choice between the element that made up the local level and the element of the global level during two 10-second test trials. Because infants aged three to thirteen months

reliably show a novelty preference, infants were expected to look longer at the element they were not biased towards during the familiarization period. T-tests and univariate ANOVA were used to compare familiarization times as well as element preference during test trial.

Results: There were no differences between the age groups for time spent looking during familiarization (p=0.271) or test trials (p=0.983). Infants twelve to thirteen months significantly prefer looking to the local element, indicating a global bias during familiarization, during the test trials (p=0.01). In contrast, three and four as well as six and seven month olds did not show a preference during test trials (p=0.294 and p=0.971, respectively).

Conclusions: Our findings suggest that by twelve and thirteen months of age, typically developing infants display a global processing bias; however, this bias is not present at three to seven months of age. Understanding developmental change in typically developing perceptual processing will inform hypotheses regarding the perceptual and cognitive mechanisms that go awry in the development of autism.

105.102 102 Associations Between Repetitive Behaviours, Play and Development in Pre-School Autism. C. Holt*, K. Leadbitter, J. Green, C. R. Aldred and .. PACT Consortium, *University of Manchester*

Background: Repetitive and restricted behaviours (RRBs) represent a key diagnostic feature of autism (DSM-IV, APA). However there is relatively little research into the incidence of these behaviours using observational methods rather than parent reports. Likewise little known about the relationships between RRBs and other areas of the autism triad and development. Previous research has found an inverse relationship between advanced play behaviours and restricted object use (Bruckner and Yoder, 2007). Similarly RRBs have been found to negatively associate with language and non-verbal development (Militerni et al, 2002).

Objectives: We used a systematic observation methodology to investigate the presence of RRBs in a standardised free play session between preschool children with autism and their caregivers; and related these to other measures of development and autism symptomology. We hypothesised that a higher incidence of RRBs would associate negatively with advanced play behaviours, language and non-verbal development, but positively with simple play and autism severity.

Methods: 51 children (mean age = 44.5 months, SD = 8.53) with autism played with their caregiver with a standardised set of toys. Coding for RRBs were modified from items used in the Repetitive Behaviour Questionnaire (Turner, 1999), DISCO (Wing et al, 2002) and Watt et al (2008). Coding of Play levels were similar to those described previously by Naber et al (2008), Belsky and Most (1981) and Leslie (1987). All coding was standaradised using The Observer (Noldus, 1991). Children also completed the Pre-School Language Scales (Zimmerman et al, 1997), Mullen Scale of Early Learning (Mullen, 1995) and the Autism Diagnostic Observation Schedule (ADOS; Lord et al, 2000). These measures formed part of the baseline assessment for the Pre-School Autism Communication Trial (PACT; www.medicine.manchester.ac.uk/pact).

Results: During a 10 minute free play sequence, children on average displayed 6.76 RRBs (SD = 7.84). The most common behaviour was "fiddling with toys" followed by "throwing and kicking." Total RRBs negatively correlated with mean language scores (r_s = -.294, p = .04) and positively with ADOS stereotyped behaviours and restricted interests (r_s = 302, p = .035). Negative associations were found between the total number of RRBs and time spent in functional (r_s = -.349, p = .014) and advanced functional play (r_s = -.287, p = .045). Total RRBs positively correlated with simple exploratory play (r_s = .326, p = .022).

Conclusions: Results suggest an inverse relationship between RRBs and advanced forms of play and development; consistent with the small amount of existing research in this area (e.g. Bruckner and Yoder, 2007). No associations were found between autism severity and RRBs, but a marginal correlation with ADOS stereotyped behaviours and restricted interests. Future work aims to explore the incidence of RRBs over time and their expression in non-verbally matched controls.

105.103 103 Onset of Repetitive Behavior/Restricted Interests and Loss of Skills in Young Children with Autism. A. Thurm*[1], S. Shumway[1], C. Lord[2] and S. E. Swedo[1], (1)*National Institute of*

Mental Health, National Institutes of Health, (2)*University of Michigan*

Background: Although onset of repetitive behaviors in autism is now known to occur as young as the second year of life (Cox et al., 2003), little is known about whether the onset of these symptoms relates to reports of skill losses in children diagnosed with autism.

Objectives: This study examined the timing of skill loss in comparison to the onset of specific repetitive behaviors in young children with autism.

Methods: Parents of 61 children (45 autism, 16 PDD-NOS; mean age 35.8 months) were interviewed with the Autism Diagnostic Interview – Toddler version to determine timing of symptom onset and loss of skills, in a study recruiting children with autism - both with and without histories of regression. The following 10 repetitive behaviors/restricted interests were examined: unusual preoccupations, circumscribed interests, repetitive use of objects/interest in parts of objects, compulsions/rituals, unusual sensory interests, difficulty with minor changes in child's routine, resistance to trivial changes in the environment, unusual attachment to objects, hand and finger mannerisms, and other complex mannerisms.

Results: Preliminary analyses find a loss of language (i.e. words, vocalizations, babbling, communicative intent, or cooing) and/or social skills (i.e. social engagement and responsiveness) was reported in 33 of the 61 children (33 with language loss, 26 with loss of social skills), with a mean age of earliest loss at 16.9 months. The average age of reported first symptoms of autism was 13.5 months for the whole group, and 14.6 for the loss subgroup.

The most commonly reported early repetitive behaviors/restricted interests were: repetitive use of objects (90%), unusual sensory interests (82%), hand and finger mannerisms (67%), and complex mannerisms (70%). The average age of onset (earliest reported) of any repetitive behavior was 14.3 months.

Of the 33 children with reported losses, 21 (64%) had reported repetitive behavior (in at least one area) at least one month prior to age of loss. Nine of the 21 children with repetitive behavior prior to loss also had this type of behavior reported by parents as a first concern, compared with none of the 12 children with repetitive behavior onset after losses. Significantly earlier ages of onset were reported for repetitive use of objects and unusual sensory interests in children with repetitive behavior prior to losses.

Conclusions: Many parents of children who reported skill losses also reported an earlier onset of repetitive behaviors, with some reporting these to be among their first concerns. These findings are consistent with reports of "lower level" or "repetitive sensorimotor" symptoms (Richler , 2007), that require fewer cognitive and language skills than others, and may be more likely to present themselves quite early. Further study should investigate how these types of early symptoms relate to reported social and communication losses, as they may provide clinicians with earlier diagnostic signals.

105.104 104 The Context of Repetitive and Stereotyped Behaviors in Young Children with Autism Spectrum Disorders: Exploring Functions. A. B. Barber*[1], N. J. Chambers[2], A. M. Wetherby[3] and L. B. Swineford[3], (1)*University of Alabama*, (2)*University of Witwatersrand*, (3)*Florida State University*

Background: Repetitive and stereotyped behaviors (RSB) are frequently interpreted in clinical settings in terms of their apparent functions. However, few studies have systematically examined the functions of RSB in children with ASD. Therefore, there is a clear need to conduct comprehensive studies of the phenomenology of repetitive behaviors seen in ASD (Lewis & Bodfish, 1998) which would have important intervention implications.

Objectives: There were three objectives of this study: 1) to describe the functions underlying RSB in young children with ASD; 2) to compare the functions demonstrated by children with ASD to children with developmental delays (DD) and typical development (TD); and 3) to examine the relationship between the functions and social and symbolic behaviors and autism symptoms.

Methods: *Communication and Symbolic Behavior Scales* (*CSBS;* Wetherby and Prizant, 2002) behavior samples were videotaped as a part of an ongoing longitudinal study of the FIRST WORDS® Project. Using Noldus Pro Observer® video software version XT, five object placement triggers, a dichotomous regulation measure, and nine function categories were created and measured within each RSB episode demonstrated

during the *CSBS* behavior sample. Children between 18-24 months of age who displayed 3 or more RSB were selected. The 161 participants included children with ASD (*n* = 55), DD in which ASD had been ruled out (*n* = 22), TD matched on chronological age (TDCA; *n* = 37), and TD matched on mental age (TDMA; *n* = 47). Group differences between object placement, emotional regulation, and functions of RSB were examined. In addition, concurrent correlations between functions and social and symbolic behavior in the 2nd year and predictive correlations between functions in the 2nd year and ASD symptoms in the 4th year were computed.

Results: Although children with ASD showed higher rates of RSB, similar object placement and function profiles were demonstrated across groups, particularly between the ASD and TD groups. Occupying self was the most common function across all groups. Self soothing and intense excitability were the least common. Children with ASD demonstrated more RSB for object focused functions than the TD groups and fewer RSB for functions related to the meaningful use of objects than children in the DD and TDCA groups. Children with ASD also demonstrated significantly lower proportions of well regulated behavior during episodes of RSB with large effect sizes than children with DD, TDCA, and TDMA.

Conclusions: These results support previous conclusions indicating that RSB may not serve a single function (Lewis and Bodfish, 1998; Reese et al., 2003; Turner, 1999) and that RSB demonstratd at this young age may appear similar in children with ASD and TD (Leekam et al., 2007). These findings offer a systematic framework within which RSB may be functionally assessed and may contribute to intervention decision-making. The findings also provide important details about triggers and functions that broaden our understanding of RSB in young children with ASD.

105.105 105 Pointing Study in Children with Autism. S. De Martino*[1], A. M. Girardot[1], C. Chatel[2], D. Da Fonseca[3], V. Rey[1] and F. Poinso[2], (1)*Autism Resource Center, EHESS & CNRS, Marseille, France*, (2)*Autism Resource Center*, (3)*INCM, CNRS; Autism Resource Center*

Background: Pointing seems to be one of the first communicative tools used by babies. It is a key part of the shared attention mechanism in child-adult interaction. It seems to emerge, in stages, and in association with oral productions. What about autistic children with verbal skills? Do they develop pointing like typical children do?

Objectives: On the basis of our preliminary findings, we propose the following hypothesis: 1/ Autistic children with verbal skills seem to develop a declarative pointing like typical children while their communication remains impaired, 2/ Declarative pointing seems to play an important role in words and sentences development even if language is not used in order to communicate.

Methods: 30 autistic developmentally delayed children, participated in this study. Patients were recruited from the « Autism Resource Centre » of Child Psychiatric Unit of Ste Marguerite Hospital in Marseille (France). Children's parents were assessed with the ADI-R (Autism Diagnostic Interview Revised). The developmental age was established with the PEP-R3. The early communication skills were assessed with the Guidetti-Tourrette scales (French adaptation of the Seibert-Hogan scales).

Results: Preliminary analysis of 30 autistic children reveals a significant correlation between declarative pointing and joint attention and another significant correlation between imperative pointing and behavioural regulation. These results indicate that declarative pointing is present in all autistic children with verbal skills and confirm our hypothesis that declarative pointing seems to be an important developmental step in language process. The autistic children, who haven't developed language yet, present just an imperative pointing.

Conclusions: We will try to establish a link between language and communication in autism. Our findings will be discussed in relation with developmental theories.

105.106 106 Adaptive Functioning as a Predictor of Treatment Success in the UCLA PEERS Program. M. J. Wang*[1], M. L. Clements[1], C. Mogil[2], A. R. Dillon[2] and E. Laugeson[2], (1)*Fuller Theological Seminary*, (2)*UCLA Semel Institute for Neuroscience & Human Behavior*

Background: Social skills training is a popular method of assisting individuals with autism spectrum disorders (ASD) to improve their social competence, yet little is known about the factors that predict successful treatment outcome.

Objectives: This study was designed to examine the impact of adaptive functioning in the

prediction of treatment outcome based on a manualized parent-assisted social skills treatment program for adolescents with high functioning autism or Asperger's disorder.

Methods: 30 adolescents with ASD and their parents participated in a 12-week manualized social skills intervention as part of the UCLA PEERS Program. Parents completed the Vineland Adaptive Behavior Scale, Second Edition (Vineland-II) at pretest and the Social Skills Rating Scale (SSRS) at pre and posttest.

Results: The change in SSRS was examined using three separate multiple regressions. In each case, posttest SSRS scores was the outcome variable, pretest SSRS scores were entered on the first step of the regression, and one of the three Vineland-II scales (Daily Living Skills, Communication, or Socialization) was entered on the second step to determine if pretest levels of adaptive functioning significantly predicted change in SSRS. Levels of adaptive functioning at pretest were not found to significantly predict change in SSRS. However, separate post-hoc analyses examining only posttest SSRS scores and adaptive functioning revealed that both Daily Living Skills ($B = 0.45$, $SE_B = 0.20$, $\beta = .39$, $p = .03$) and Communication Skills ($B = 0.83$, $SE_B = 0.37$, $\beta = .39$, $p = .03$) significantly predicted social skills functioning at posttest, but Socialization did not ($B = 0.38$, $SE_B = 0.31$, $\beta = .22$, $p = .23$).

Conclusions: This study sought to investigate predictors of treatment success for a parent-assisted social skills intervention. Although adaptive behavior does not appear to predict the amount of change in improvement of social skills over the course of treatment, specific components of adaptive behavior, such as daily living skills (e.g., the ability to complete weekly socialization homework assignments) and communication skills (e.g., the ability to carry on a conversation), do appear to predict level of social skills functioning following treatment.

105.107 107 Social Skills Training for Preschool Children with Autism Spectrum Disorders: The UCLA PALS Program. J. Sanderson*[1], Y. C. Chang[1], R. W. Ellingsen[2], A. R. Dillon[1], F. Frankel[1] and E. Laugeson[1], (1)*UCLA Semel Institute for Neuroscience & Human Behavior*, (2)*University of California, Los Angeles*

Background: Although social skills training has become an increasingly common approach in improving the social deficits found in young children with Autism Spectrum Disorders (ASD), few interventions use valid and reliable standardized assessment measures to evaluate treatment efficacy. In addition, most intervention studies in this area have a small sample size, involve school-aged children, and/or do not use multiple raters to assess treatment efficacy.

Objectives: This study examines the efficacy of a manualized social skills intervention, known as the UCLA Preschool Applied Learning of Social Skills (PALS) Program, in improving overall social skills among preschool children with Autism Spectrum Disorders.

Methods: 10 children completed the PALS intervention over a period of 15 weeks as part of their enrollment in an intensive therapeutic social recreational program for children 3-6 years of age diagnosed with high-functioning autism, Asperger's Disorder, or PDD-NOS. Prior to receiving the PALS intervention, parents and teachers rated the participants' social skills, problem behaviors, and social responsiveness using the Social Skills Rating System (SSRS; Gresham & Elliot, 1990) and the Social Responsiveness Scale (SRS; Constantino, 2005). Participants receiving the PALS intervention attended 20 minute manualized treatment sessions 2-3 times per week and participated in several structured games and activities throughout the week involving behavioral rehearsal of the targeted skills. Parents received weekly handouts describing the social skills lessons as well as strategies for reinforcing these skills in the home and community setting. Targeted social skills included: social communication and conversational skills; turn-taking and sharing; peer entry skills; good sportsmanship and teamwork; helping behavior; and appropriate body boundaries. Skills were taught through puppet-facilitated scripted didactic lessons using concrete rules and steps of social etiquette followed by role-playing exercises by group leaders and peer models. Participants practiced newly learned skills during structured and unstructured behavioral rehearsal exercises with peers. Following the 15 week intervention, parents and teachers again completed the SSRS and SRS to assess for treatment outcome.

Results: Findings reveal significant improvement on parent report of social responsiveness on the SRS ($p = 0.006$) following the treatment

intervention. Further analysis of the SRS revealed significant improvement on parent report of three subscales, including Social Awareness (p = 0.031), Social Cognition (p = 0.019), and Social Motivation (p = 0.007). Examination of the SSRS indicated significant improvement on teacher report of Assertiveness (p =0.042), and trends in parent-reported increased Self Control (p = 0.057), parent-reported decreased Hyperactivity (p = 0.066), and parent-reported decreased Problem Behaviors (p = 0.058) following the treatment intervention. Parent report of overall social skills and teacher reports of problem behaviors, overall social skills, and social responsiveness were not significant.

Conclusions: These findings suggest that the use of PALS, a manualized social skills treatment intervention, may be efficacious in improving the social responsiveness of children with ASD along the dimensions of social awareness, cognition, and motivation, and may improve their assertiveness in the classroom setting.

105.108 108 Peer Relationships of Children with ASD in General Education Settings. A. Gulsrud*[1], J. Locke[1], E. Rotheram-Fuller[2] and C. Kasari[1], (1)*University of California, Los Angeles*, (2)*Temple University*

Background: Many children with autism are included in the general education classroom. Little is known about the social relationships that exist between children with autism and their typical peers in the classroom.

Objectives: This study examined the social connections between peers in general education classrooms when one of the peers had an autism spectrum disorder. Children's acceptance, reciprocity and self-reports of friendship quality were examined for first to fifth graders.

Methods: Sixty, first-to-fifth grade children with autism participated across 56 classrooms in 30 different schools in a large urban city. These children were compared to a matched sample of typical children from the same classroom, same gender, and same age. Of the children with autism, 16 children were in first grade, 17 children in second grade, eight children in third grade, 11 children in fourth grade, and eight children in fifth grade. Children with autism were from diverse ethnic backgrounds (46.7% Caucasian, 5% African American, 21.7% Latino, 16.7% Asian, and 10% Other) and were predominantly male (90%). All were fully included in regular education classrooms and were an average of 8.14 years old (sd=1.56), with an average IQ of 90.97 (sd=16.33). Typically developing children were an average of 7.87 years old (sd=1.42). Measures included a sociometric measure of children's friendships based on peer nominations (Cairns & Cairns, 1994), a self-report questionnaire of friendship quality (FQS; Bukowski, Hoza & Boivin,1994) and playground behavioral observations.

Results: Outcome measures of social network status and friendship quality were analyzed using mixed-effects linear models. Results indicated that the children with autism had significantly fewer social connections in the classroom (1.36 ± 0.1) as compared to their typically developing matched peers (2.16 ± 0.1), $F(1,4) = 33$, $p<.01$. Thus, children with autism nominated significantly fewer children (3.9 ± 0.36) from their classroom as friends than typically developing children (5.4 ± 0.37), $F(1,4) = 9.06$, $p<.05$. In addition, children with autism received significantly fewer friendship nominations from classmates (1.4 ± 0.25) than their matched peers (3.1 ± 0.25), $F(1,4) = 21.90$, $p<.01$. Also the proportion of children's reciprocal friendships was significantly lower in children with autism (18.1% ± 5.58) in comparison to their typically developing matched peers (64.1% ± 5.39) $F(1,4) = 35.12$, $p<.01$. When examining children's number of rejections, there was no significant difference between the number of rejections received in children with autism and their matched peers.

Children with autism reported significantly poorer friendship quality in the domains of companionship ($F(1,4)=8.00$, $p<.05$), help ($F(1,4)=12.94$, $p<.05$) and closeness ($F(1,4)=15.52$, $p<.05$). They did not have significantly different ratings in the domains of security or conflict; $P>.05$).

Conclusions: This study shows that children with autism in general education settings are self-reporting poorer friendship quality than their typical classmates and these findings are validated by the typical children's lower ratings of social functioning for children with autism on the sociometric questionnaire. These results provide additional information about the social development and competence of children with high functioning autism and demonstrate that

systematic social skills interventions are needed in the public schools.

105.109 109 Designing Social Competence Progress Monitoring through Curriculum Based Measures: a Pilot Study. J. Stichter* and C. Schmidt, *Thompson Center for Autism and Neurodevelopmental Disabilities*

Background: Youth with ASD experience social competence deficits that impact their ability to make and sustain friendships, initiate and maintain social interactions, and understand emotions in themselves and others. Without targeted intervention services, these youth often exhibit problematic social behaviors and can become socially withdrawn, which negatively impacts their quality of life and can lead to other developmental skill deficits. In order to adequately evaluate program interventions for individuals with ASD, valid and reliable assessment of progress is mandatory. CBMs are evaluation tools that measure participant growth and progress across curricular constructs (Deno, 1985). CBMs assess the participant's skill level at specific probe periods during the instructional sequence, and determine what skills may be emerging as the curriculum scaffolds learning across the units (Rubin & Laurent, 2004). To date, our measures are the first use of the CBM format in a non-academic area, the area of social competence.

Objectives: We developed our CBMs based on the criteria established for academic CBM (Deno, 2003) which includes: immediately sensitive to small changes in instructional interventions, reliable, easy to administer, numerous forms that can be administered to the same student, time efficient, inexpensive to produce, unobtrusive to instruction, simple to teach. This study piloted the use of CBM to monitor the progress of participants in our Social Competence Intervention-Cognitive Behavioral Intervention (SCI-CBI) program. Methods: The CBM consists of five sections developed to represent the general constructs in each of the five (SCI-CBI) curricular units. During the ten-week intervention, the full suite was administered at pre- and post-assessment and at the conclusion of each two-week unit. Specific CBM items were rotated and varied to ensure that students would not be exposed to the same item, though the same constructs were assessed multiple times throughout the intervention.

Results: The current sample includes 8 boys (age 11-14.75 years; mean full scale IQ = 97.1) diagnosed with an ASD who participated in the most recent administration of the SCI-CBI program. Overall, results indicated significant change between pre and post assessment scores (expressed as a percent change) on multiple global measures (SRS mean change = 20.3, $t=5.19$, $p<.01$; TOPS mean change = 8.8, $t=-2.71$, $p<.05$; BRIEF mean change = 10.8%, $t=5.13$, $p<.01$). Students also evidenced growth on the CBM (13.8% on the total score), though this change was non-significant. Finally, as with previous iterations of the CBM, we found some significant association between growth on the CBM and SRS (CBM facial expression recognition and SRS total, $r=.73$, $p=.06$). Additional students will participate in the program in Spring 2009, thus the data presented here is preliminary.

Conclusions: Results indicate the possible utility of CBMs in applied settings as an efficient, applied progress-monitoring tool to capture discrete changes in social behavior for individuals with autism spectrum disorders.

105.110 110 Differentiated Effects of Two Social Story™ Formats, Paper Versus Computer Assisted, on Aberrant Behavior in Children with Autism. G. R. Mancil*[1] and P. Schaefer Whitby[2], (1)*Kelly Autism Program at Western Kentucky University*, (2)*University of Central Florida*

Background: Social Stories™ are short stories often written for children with Autism Spectrum Disorder (ASD) to help individuals understand social situations (Gray, 1998) and many times results in the development of the necessary behavioral skills to engage in specific social activities (Crozier & Tincani, 2007; Scattone, Tingstrom, & Wilczynski, 2006). Despite evidence from previous studies that support using social stories on problem behaviors, researchers have recommended utilizing more rigorous controls to examine whether or not Social Stories is an evidence-based practice. Objectives: Determine the effectiveness of two social story™ formats on aberrant behaviors of children with ASD. In addition, determine the difference between the effects of a paper format versus the computer format was analyzed. Finally, determine the generalization of the skill across environments. Methods: The subjects were referred by a local autism center that provides services for children with autism spectrum disorder and their parents. The subjects' diagnosis of ASD was confirmed by a review of records and the completion of the ADI-R. The same social story was written for the three

subjects in two formats, one paper and one interactive Powerpoint™. The researcher trained the subjects' respective teachers how to implement the social stories. The teachers described the story to their prospective students (i.e., subjects). The participants then read the story. After each student read the story, the teachers checked for understanding. The questions were standardized across participants. When the targeted students responded correctly to all of the questions, the intervention phase began. An ABABCBC multi-component reversal design was used for each participant (Kennedy, 2005). This design was selected because it allowed for replication of intervention effect within each participant, enhancing internal validity of the experiment. In addition, this design allowed for the comparison of the PowerPoint ™ Social Stories to baseline and to the paper format social stories. Thus, allowing for functional relation statements to be made. Results: The results indicated a decrease in the frequency of aberrant behavior for each subject. Outcomes were slightly better for the PowerPoint ™ format than paper format. Further, the results maintained across the training setting, indicated the skill could be generalized to other settings with a single prompt, and social validity assessments indicated that the PowerPoint ™ format was easily implemented and preferred by both teachers and subjects (i.e., students). Conclusions: In conclusion, findings of the present study contributed to the Social Story literature because it examined and compared two social story presentation formats and demonstrated that the social story decreased aberrant behaviors. In addition, the present study extended the literature by accessing maintenance and generalization of the social story and social validity from the participants.

105.111 111 Discourse Processing in Autism: Effects of Linguistic Connectives. D. L. Williams*[1], R. A. Mason[2] and M. A. Just[2], (1)*Duquesne University*, (2)*Carnegie Mellon University*

Background: Previously we reported a study examining the intersection of Theory of Mind (ToM) processing with narrative discourse comprehension in autism (Mason et al, *Neuropsychologia,* 2008). The results of that study suggested that although the ToM network was activated in individuals with autism, it was inefficient. Whereas the control participants selectively activated a ToM network only when appropriate, the autism group processed all inferences similarly; they used the ToM network even when no additional ToM processing was required. The cortical system in autism appears to meet the cognitive challenge created by discourse processing by indiscriminately engaging RH language and ToM areas. This previous study did not have any explicit linguistic cues forcing the reader to causally link the presented information. We were interested in the further study of discourse processing in high-functioning individuals with autism.

Objectives: To investigate whether the brains of individuals with autism always responded in a similar manner during discourse processing or whether the processing was sensitive to two different types of textual information: 1) linguistic cues that explicitly invited integration of information; and, 2) whether the inference was moderately or distantly connected to the textual information.

Methods: Participants complete a reading task presented via computer while lying in a 3T Siemens Allegra magnetic resonance imaging scanner. Stimuli consist of 40 reading passages, 10 in each of 4 conditions in a 2 X 2 design: moderately- vs. distantly-related inference and the presence or absence of one of four connectives (thus, hence, consequently, and therefore). Participants are high-functioning adults with autism and age and IQ-matched controls with Full Scale and Verbal IQs ³ 80. Standard fMRI analysis measures are being performed including group comparisons of regions and significant levels of activation in the experimental conditions. Functional connectivity differences by group and condition will also be examined.

Results: The behavioral, functional imaging, and functional connectivity data from approximately 25 individuals with HFA and 25 age and Verbal IQ-matched controls will be presented.

Conclusions: The predictions we are testing are that the autism group will activate ToM network and language processing networks during the moderately-related discourse processing condition, indicating some integration of information. However, these networks may be recruited less during the distantly-related condition as the autism group treats the information as unrelated text. Explicit cuing may change this processing pattern, forcing integration in the distantly-related passages that was not previously observed. Processing of explicit cues may also be reflected in an increase in frontal-

posterior functional connectivity as compared to the condition without linguistic cues.

105.112 112 Investigating Peer Interaction during Play in Children with Autism Using a New Ecologically Valid Paradigm. D. Simon*[1], S. P. Mendoza[2] and B. Corbett[1], (1)*M.I.N.D. Institute, University of California at Davis*, (2)*University of California, Davis*

Background: Children with autism often exhibit deficits in social interaction including spontaneous play behavior with peers. While the specific nature of these deficits is well documented there is a lack of research into the contexts and temporal relationships of interactions and behaviors that most acutely manifest them.

Objectives: The current study was designed to examine social behavior between typically developing children and those with autism using an ecologically valid playground setting. In addition to traditional analysis based on examining frequency and duration of target behaviors, a transactional analysis of temporal and context based information was employed. The transactional method allows examination of events both in terms of time (i.e., temporal context, chronolology) as well as behavioral sequences (i.e., response circumstances, responses across multiple participants). As a result, the method can reveal relationships between superficially unrelated behaviors based on contextual clues.

Methods: The pilot study included 27 children ages 8-to-12 years of age with autism (n=13) and typical development (n=14) that participated in a peer interaction paradigm. Each twenty minute playground sequence included three children: a neurotypical child, a neurotypical confederate and a child with high functioning autism. Recording was accomplished via four cameras, with combined coverage of all playground areas, and lavalier microphones worn by each participant. Sound and video mixed records were subsequently coded using Noldus software. A sophisticated, detailed coding of interaction and play sequences was developed for this investigation. Multivariate and univariate analyses of variance were used.

Results: Children with autism engaged in fewer interactions during solicited gross motor and directed play than neurotypical children $F(1,25) = 4.21$, $p<0.05$ and less cooperative play $F(1,25)=4.12$, $p<0.05$. No differences were found in overall gesturing or avoidant behavior. It is important to note that observed unequal variances suggest increased variability in some aspects of social responsivity in the autism group.

Conclusions: The findings indicate reduced interactivity in children with high functioning autism and these patterns more intensely manifest during periods featuring solicited interaction from the neurotypical peers. The data further suggests that within the autism group, subgroups emerge revealing distinct social interactivity profiles. The behavioral results will be compared to biological indices of stress and symptom profiles as part of a larger study.

105.113 113 Using the ADI-R Diagnostic Intervew to Profile the Phenotypic Characteristics In ASD. M. Foscoliano[1], P. Cavolina[1], G. Putzolu[1], S. Vacca[1], R. Fadda[2] and G. Doneddu*[1], (1)*A.O.B. (Azienda Ospedaliera Brotzu)*, (2)*University of Cagliari*

Background: Many studies have sought to improve the power of their analysis by increasing sample size, stratifying groups to improve phenotypic homogeneity and performing linkage analysis to quantitative traits related to phenotypic components of Autism Spectrum Disorders (ASD) (Hus V., Pickles A., Cook E., Risi S., Lord C., 2007).

Objectives: In line with previous research the purpose of this study was to identify similiraties and differences of phenotypic characteristics (ADI-R domains, NVIQ, age, sex) in children with ASD, considering alternatively the 3 ADI-R domains: Communication, Social Reciprocal Communication and Restricted and Repetitive Behaviours.

Methods: We analysed 92 ASD children (diagnosis: 54 Autism, 31 PDD-NOS, 7 Asperger syndrome), 79 males and 13 females, ages 2 to 15 years, (aver. chron. age 6,6; sd 3,3). Parent were asked to complete the ADI-R while each child was evaluated using the Leiter-R.

Results: Considering the Communication domain we found higher restricted and repetitive behaviours in children above the cut-off (>cut-off aver. score 6,1; sd 3,4; cut-off aver. score 16,6 - sd 6,9;
Evaluating the Social Reciprocal Communication domain, there were higher restricted and repetitive behaviours (>cut-off aver. score 6,1; sd 3,4; cut-off aver. score 76,8; sd 22,7; cut-off aver. score 23,9; sd 15,6; In the Restricted and

Repetitive Behaviours domain subjects showed an higher impairment on communication, a more pronounced stereotyped and repetitive language (> cut-off aver. score 2,4; sd 2,1; cut-off aver.score average 77,7; sd 22,8; cut-off aver. score 2,8; sd 2; cut-off aver. score 11,8; sd 5,2; < cut-off aver. score 8,9; sd 5,3; F= 4,819; p=0,031).

Conclusions: In general, the analysis of the single domain of ADI-R highlighted the distinct phenotypic charateristics in ASDs. In particular, the group with Restricted and Repetitive Behaviours seems to be characterized of a lack of early social ablity (eye conctact and social smile) and an higher impairment on verbal communication.
In the group that had a higher cut-off in the Social Reciprocal Communication domain, the low NVIQ might play a central role that need to be more investigated.
Moreover, these results might be used to drive more effective and individualised intervention.

105.114 114 Performance of Children with Autism Spectrum Disorders and Children with Pragmatic Language Impairment on an Emotion Recognition Task. L. M. Reisinger*[1], K. Cornish[2] and S. Williams[2], (1)*Montreal Children's Hospital*, (2)*McGill University*

Background: This study examines emotion recognition ability in children with Autism Spectrum Disorders (ASD) and children with Pragmatic Language Impairment (PLI). Children across the autism spectrum, irrespective of cognitive functioning or categorical separation, all share a similar linguistic profile that includes a delay in pragmatic language. Pragmatic language impairment results in delayed ability to use language appropriately in a given context. It has also been linked with significant difficulty interpreting other people's behavior and impaired social interaction. This social/linguistic profile is seen in both children with pragmatic language impairment and children with autism spectrum disorders. **Objectives:** The objective of this study was investigate whether there is a syndrome group difference in emotion-recognition discrimination ability in high functioning school-age children with Autism Spectrum Disorders (ASD), children with Pragmatic Language Impairment (PLI), and typically developing children who are matched on language age and IQ. **Methods:** Participants included 22 school-aged children diagnosed with autism spectrum disorder (mean age = 10.2), 19 children with pragmatic language impairment (mean age = 9.6), and 35 typically developing comparisons (mean age = 10.5) (N=76). Participants had fluid language and an IQ above 80. All participants were tested on the children's version of the *Mind in the Eyes* emotion recognition test. Cognitive ability and direction of eye gaze in the stimuli photos was controlled for in the analysis of the data.**Results:** When controlling for IQ, performance of the disorder groups differed significantly from typically developing comparisons when the person in the test photograph was *thinking* about an emotional event (e.g. "thinking about something sad"). Atypical groups did not differ from the comparison group on emotions identified as being felt directly by the person in the photograph (e.g. "feeling sad" or "feeling happy"). IQ had a significant influence on the ability to recognize emotion for all groups. No significant relationships were found between direction of eye gaze and ability to recognize emotion. **Conclusions:** The pattern of findings suggest that IQ has the greatest influence on the ability of children with ASD and PLI to recognize emotion, with lowered IQ scores increasing the probability of misinterpreting emotions displayed in the eye region of the face. This study has provided more evidence that children with Autism Spectrum Disorders, who have fluent language and an average IQ, do not have the significant impairments in emotion recognition, previously thought to be displayed by this group. Diminished abilities are present in both children with Pragmatic Language Impairments and children with Autism Spectrum Disorders, when the emotions being displayed represent past emotions.

105.115 115 Behavioral Regulation and Risk Taking in High-Functioning Autism. J. Dana*[1], S. E. White[1], A. Cariello[1], M. J. Crowley[2] and M. South[1], (1)*Brigham Young University*, (2)*Yale University*

Background: Response to emotion plays an essential role in decision making. In general, previous research has shown that although individuals diagnosed with Autism Spectrum Conditions (ASC) have difficulty with many cognitive tasks, they do respond to the manipulation of emotional influences on cognitive tasks in similar ways to comparison groups. In typical development, styles of behavioral regulation of emotion have been shown to be related to sensitivity to risk and reward in

laboratory settings. We wondered how the behavioral regulation of emotion in ASC influences decision making.
Objectives: Based on the small existing literature, we hypothesized that although ASC individuals may not perform as optimally as typical comparison groups on a risk-based decision making task, the relative relationships between behavioral regulation and response to risk and punishment would be intact in ASC. That is, cognitive factors (including generally slower reaction time and longer time to process or integrate all of the available information) would lead to impaired performance overall, but that correlations between risk-taking and behavioral inhibition and activation would be similar to the comparison group.
Methods: 50 adolescents and adults (25 ASC and 25 matched comparison) completed the Balloon Analogue Risk Task (BART), a computer-based task that requires the participant to "blow up" virtual balloons as large as possible (in order to gain points) without popping them. Participants also completed the appropriate (child or adult) version of the BIS/BAS questionnaire regarding behavioral regulation style; parents of adolescents completed the parent version. Galvanic skin response (GSR) and heart rate (HR) data were collected simultaneously during the BART task via disposable electrodes on the fingers, wrist, and ankle.
Results: Both the ASC and comparison groups demonstrated substantial within-group individual differences regarding the value (relatively high, low, or medium) of their early responses. Both groups showed significant learning during the BART task as evidenced by a move from more extreme early responses towards successful, mid-range responses for the duration of the task. The ASC group took slightly longer to achieve this point: the median response was achieved between the 13th and 14th (of 30) trial, about 2 trials longer than the comparison group. Both groups demonstrated significant correlations between total earnings for the task and both the Behavioral Activation System-Drive Scale (positive correlation) and the Behavioral Inhibition Scale (negative correlation); these correlations were especially strong (>.55) for earnings during the early (first 10 trials) portion of the task. The BAS-Reward scale was significantly, positively correlated with the GSR difference score for rewarded versus punished trials, reflecting a relationship between risk-taking on the BART task and the behavioral measure; this correlation was not significant for the ASC group.
Conclusions: There does appear to be a significant relationship in ASC between style of behavioral regulation of emotion, and performance on a risk-based experimental task. However, this may be moderated by different physiological mechanisms. There is a bright future for research regarding emotional and cognitive endophenotypes of ASC using a combination of survey, experimental and physiological techniques.

105.116 116 Emotional Mimicry and Contagion in Children with Autism, Down Syndrome and Typical Development. K. Hudry*[1] and V. Slaughter[2], (1)*Institute of Education, University of London*, (2)*University of Queensland*

Background: Affective and empathic impairments have long been recognised in Autism Spectrum Disorders (ASD). To date, however, research has tended to focus on higher-level processes of empathic and prosocial responsiveness, with little attention yet given to the earlier emerging forms of emotional mimicry/contagion. Typical empathic development is proposed to begin with neonatal contagious crying, which is gradually replaced by empathic concern and prosocial helping. As with crying, laughter also typically develops under minimal conscious control, and becomes readily 'contagious'. This form of contagion, however, remains through adulthood. Objectives: Given the well-established deficits in empathic responsiveness in ASD, and the proposed developmental link between higher-level empathy and lower-level forms of emotional mimicry/contagion, investigation of contagion responses in ASD should serve to further inform the precise nature emotional deficits in this condition. The current study presented young children with ASD and matched controls with live stimuli designed to elicit varying degrees of empathy and contagious responses. Differential responding between children with ASD and controls would suggest a basic affective impairment in this condition, whereas similar responding would suggest that emotion only becomes impaired at higher-levels. Methods: Participants were 69 young children (aged between 23 months and 8 years 2 months) with ASD, Down syndrome or typical development. Within a play session, several emotional scenarios were presented; a replication of Sigman et al.'s (1992) pain scenario to assess empathy, and two novel scenarios to assess emotional mimicry/contagion (an adult laughing and the

sounds of an infant crying). Children's responses were coded for duration of attention toward the emotional displays, duration of congruent affective displays (i.e., positive or negative expression), and evidence of contagious emotion (i.e., child crying or laughter, as appropriate). Results: In line with past research, the children with ASD were significantly less empathic than controls, looking less toward the adult in pain. Across all groups, however, children were not particularly negative, upset, or prosocial in their responsiveness. Children with ASD were similarly less attentive than controls toward the display of adult laughter. However, despite this lack of attention, they equally often displayed congruent positive affect and contagious laughter as did controls. Finally, the children with ASD were equally attentive toward the sound of infant cries as were controls, with children in all groups equally likely to approach to investigate the source of the sound, and to show negative facial affect. Conclusions: This study replicates previous findings of a higher-order empathy deficit (i.e., in responding to the pain scenario) in children with ASD. By contrast, children with ASD were found to show greater responsiveness during the scenarios of adult laughter and infant cries. This suggests that while empathy is impaired in ASD, at some base-level, emotional mimicry/contagion is spared. Further research should seek to replicate this finding, which has implications for our understanding of emotional functioning in ASD, as well as for the typical developmental link between mimicry/contagion responses and higher-order empathy skills.

105.117 117 Person Centered Employment: Increase in Job Satisfaction, Productivity, and Decrease in Challenging Behaviors for Adults with Severe Autism. T. Todd*[1], T. Kozloff[2] and B. Fields[2], (1)*California State University*, (2)*California Vocations, Inc*

Background: Seventy-five percent of adults with ASD, in the USA, are unemployed. Unemployment has social, psychological, and economic consequences. Supporting adults with severe autism in employment can be a challenge due to poor communication skills, lack of social awareness, and the presence of challenging behaviors. In addition, there is little choice in job type for these individuals. Person centered planning has been found effective in decreasing challenging behaviors for adults with autism in supported living environments, this approach may also be useful in finding successful employment opportunities.

Objectives: To increase employment satisfaction, productivity, and decrease challenging behaviors for individuals with severe autism and challenging behaviors through person centered planning for employment.

Methods: Twenty-five individuals with autism attending a recycling work shop, as well as community integration personnel (CIP) were interviewed, over a period of a year, to understand employment interests and abilities. Parents and guardians were involved when possible. Incidences of aggressive, destructive, and self-injurious behaviors were recorded for each participant. The number of incidence reports of problem behaviors from 3 six month periods during the recycling work shop were compared to the number of incidence reports during three 6 month periods of person centered employment. Number of hours spent in paid employment per year was compared from the recycling workshop to person-centered employment for each individual. Paired T-tests with Bonferrini Inequality correction were performed to determine if the change was significant. Surveys regarding program satisfaction were given to individuals attending the program, families and conservators of consumers, and regional center case workers after one year of person-centered employment. Results: Interview results were analyzed and compared for common interests and abilities. Nine micro-businesses were formed and several individuals were supported in employment at a tree farm and local major chain department store. Aggressive, destructive, and self-injurious behaviors decreased significantly when individuals were able to work in preferred employment. Number of hours spent in paid employment increased with the development of micro businesses and supported employment. Survey results were positive with regard to happiness and ability to participate in decision making. Conclusions: A person centered approach to matching employment to interests and abilities of adults with severe autism and challenging behaviors was successful in increasing time spent in employment and decreasing challenging behaviors. A decrease in problem behaviors may have a beneficial impact on the life of the individual. Individuals in the program, their conservators, families and case workers reported a high degree of satisfaction with the program.

105.118 118 The Effects of Task Demands on Self-Monitoring for Higher Functioning Children with Autism. K. E. Ono*[1], H. A.

Henderson[1], L. Mohapatra[2], C. Hileman[1], M. Jaime[1], N. Kojkowski[1], C. Schwartz[2] and P. C. Mundy[3], (1)*University of Miami*, (2)*Graduate Student*, (3)*UC Davis*

Background: It has been proposed that perseverative responding and the inability to adapt to social situations may reflect an underlying impairment in self-monitoring in individuals diagnosed with Autism Spectrum Disorder (Mundy, 2003; Henderson et al., 2006). Self-monitoring includes the ability to detect and correct errors.

Objectives: In the current study, the effect of stimulus type (non-social versus social) on post-error slowing, a behavioral index of self-monitoring, was examined among a sample of children diagnosed with High Functioning Autism and an age- and IQ-matched comparison sample.

Methods: Preliminary data are presented on 46 ASD and 45 age- and Verbal IQ-matched comparison children, between the ages of 9 and 17 who completed the Eriksen Arrow Flanker task. To-date, 27 ASD and 39 comparison children have also completed the Faces Flanker task. In the tasks participants were presented with a horizontal array of either 5 arrows (Arrow task) or 3 faces (Faces task). Participants were instructed to attend to the center stimuli, and to press a key corresponding to either the direction of the arrow or affect of the face. The dependent variables of interest for each task are (1) reaction time (RT) on correct trials following correct vs. error trials and (2) the number of correct vs. error responses on the trial following an error.

Results: On the Arrows task, a 2 (preceding trial: correct vs. error) x 2 (diagnostic group: HFA vs. comparison) repeated measures ANOVA with RT on correct trials as the dependent variable showed that RT was unrelated to preceding trial or diagnostic group. In contrast, on the Faces task a comparable analysis revealed an interaction between preceding trial and group, $F(1, 64)=4.82$, $p=.03$, $\eta_p^2=.07$. Specifically, children with HFA responded faster post-error than they did post-correct, $t(26)=2.57$, $p=.02$, whereas RTs did not differ based on the previous trial for children in the comparison sample. Response accuracy following error trials was analyzed with a 2 (diagnostic group: HFA vs. comparison) x 2 (accuracy: error vs. correct) repeated measures ANOVA. On both tasks, performance following an error was predicted by an interaction between group and accuracy, $F(1, 78)=6.75$, $p=.01$, $\eta_p^2=.08$ (Arrows) and $F(1, 55)=4.43$, $p=.04$, $\eta_p^2=.08$ (Faces), such that HFA children were more likely to repeat errors compared to comparison children, $t(78)=2.42$, $p<.001$ (Arrows) and $t(55)=1.23$, $p=.04$ (Faces). While comparison children made more correct than error responses following errors on both tasks, the HFA children only reliably corrected themselves on the Arrows task, $t(89)=2.02$, $p=.04$, but were unable to do so on the Faces task, $t(64)=.59$, $p=.45$.

Conclusions: Regardless of task, the HFA children seem to have more difficulty self-monitoring. Performance seemed particularly affected when stimuli were social, where children with HFA decreased their RT, or sped up, following an error, and were more likely to make repeated errors. These findings suggest that response monitoring may be particularly impaired in social contexts and may underlie some of the difficulties HFA children have with reciprocal social interactions.

105.119 119 Stereotypic and Repetitive Behaviour in Individuals with Autism Spectrum Disorder: a Systematic Review of Intervention Practices. S. Y. Patterson*, V. Smith and M. Jelen, *University of Alberta*

Background: A demonstration of stereotypic and repetitive behaviour (SRB) is one of three criterion required to receive a diagnosis of autism (APA, 2000). Behaviours may include restricted interests, repetitive movements or intense, constant interest in parts of an object (APA, 2000). When SRBs become so intrusive that they affect a child's ability to attend, learn and interact they require intervention. A systematic review utilizes a replicable procedure and provides unbiased and transparent quantitative and qualitative information. Evaluation of studies that use a systematic methodology aid in determining which interventions are supported by evidence to ensure that best practices are put forth for use by intervention providers. This form of review has yet to be completed in the area of SRB interventions for individuals with autism. Objectives: The objectives of the review were to: 1) identify the intervention practices used to reduce SRBs in individuals with ASD; 2) describe the participants, outcomes and intervention methods; 3) evaluate the methodological quality of the empirical evidence. Methods: A systematic search of 20 electronic databases was completed. Sixty-four studies were included after examination by two independent reviewers who applied the following

inclusion criteria: 1) interventions focusing on SRBs; 2) participants of any age diagnosed with Autism, Asperger's Syndrome or Pervasive Developmental Disorder; 3) study design was either a randomized control trial (RCT), quasi group or single case experimental design; 4) published from the year 1994 onward in English. Methodological quality was assessed. Studies underwent a quality assessment to evaluate aspects of participant selection/attrition, comparison groups, design, application of the intervention, and analysis (AACPDM, 2004; Gersten et al., 2005; Jadad et al., 1996). Data was systematically extracted and reported in evidence tables. Further, studies were classified according to the continuum of interventions for ASD including biologically based, behavioural, therapy based, reinforcement based, sensory, exercise based, restricted interests as a component of the intervention, developmental and other interventions (Roberts & Prior, 1996). Characteristics of these studies were summarized using descriptive statistics and reported by category of intervention. Results: The majority of the participants were American, Caucasian, school-aged males with a diagnosis of autism. A wide range of SRBs were examined including repetitive movement, vocalizations, self-injurious behaviours and echolalia typically in school or home settings. Overall, the methodological quality of the RCTs (n=14) was moderate to strong. Quasi group designs (n=7) were found to be of low quality and single case designs (n=43) were of moderate quality. Interventions evaluated using group designs were primarily biologically based, while single subject interventions were reinforcement and therapy based. Short term positive effects have been demonstrated for the majority of interventions however, no intervention has enough empirical support to be considered an evidence-based practice (Reichow, Volkmar & Cicchetti, 2007). Conclusions: Results indicate a variety of interventions are in place; however, only preliminary evidence exists to support their implementation. Increased methodological rigor is required in future research to determine evidence-based practices.

105.120 120 Characterizing Repetitive, Stereotyped, and Sensory Behaviors in Toddlers with Autism, Developmental Delay and Typical Development. J. Greenson*[1], J. Munson[1], J. Lindsey[1], J. Varley[1] and G. Dawson[2], (1)*University of Washington*, (2)*Autism Speaks, UNC Chapel Hill*

Background: Repetitive/stereotyped behaviors are crucial to the diagnosis of autism. However, data are needed to clarify the specificity of these features to autism and to evaluate the validity of assessment strategies in young children.

Objectives: We sought to characterize repetitive/stereotyped behaviors and sensory issues in toddlers with autism (n=60), developmental delays (DD; n=21), and typical peers (n=20). Among children with autism, we examined the association between repetitive behaviors, sensory issues, social impairment, and cognitive functioning. Finally, we examined correlations between parent reported repetitive behaviors and examiner observation.

Methods: Participants included toddlers ages 18-30 months recruited from community pediatricians and agencies. Participants were evaluated for autism using the ADOS-Module 1 and ADI-R Toddler. Repetitive behaviors and sensory issues were assessed using parent reports on the Repetitive Behavior Scale (RBS) and the Short Sensory Profile (SSP), and with examiner ratings on the ADOS. Cognitive ability was assessed using the Mullen Scales.

Results: Toddlers with autism exhibited more repetitive behaviors than children in the DD ($p<0.01$) and typically developing groups ($p<0.01$). Toddlers with autism showed more sensory issues than typical peers ($p<.01$), but this did not distinguish children with autism from those with DD. In the autism group, repetitive behaviors were predictive of greater social impairment on the ADI-R and ADOS and lower cognitive scores on the Mullen. Parent report and examiner observations of repetitive behavior were moderately correlated ($r = .28$ to $.489$).

Conclusions: Repetitive behaviors differentiated toddlers with autism from those with DD and typical peers, and were associated with greater impairment within the autism group. Toddlers with autism and DD both displayed more sensory issues than typical peers. Clinically, this suggests that repetitive behaviors, but not sensory issues, are important in distinguishing toddlers with autism versus DD. Parent report was correlated with clinician ratings, suggesting utility for initial screening.

105.121 121 Developmental Trajectories of Repetitive Behaviors in Young Children with Autism Spectrum Disorders. P. Mirenda*[1], I. M. Smith[2], P. Szatmari[3], S. E. Bryson[2], E. Fombonne[4], W. Roberts[5], T. Vaillancourt[6], J. Volden[7], C.

Waddell[8], L. Zwaigenbaum[7], S. Georgiades[9], A. P. Thompson[3], E. Duku[3] and .. Pathways in ASD Study Team[9], (1)*University of British Columbia*, (2)*Dalhousie University/IWK Health Centre*, (3)*Offord Centre for Child Studies, McMaster University*, (4)*McGill University*, (5)*University of Toronto*, (6)*University of Ottawa*, (7)*University of Alberta*, (8)*Simon Fraser University*, (9)*Offord Centre for Child Studies & McMaster University*

Background: Recent research suggests that the restricted and repetitive behaviors (RRB) domain is composed of at least two symptom dimensions in young children with autism spectrum disorders (ASDs). However, to date most studies of RRB have been descriptive or cross-sectional rather than longitudinal in nature, which limits our understanding of how these behaviors are related to other developmental factors over time. In addition, most studies have been done with samples across a wide age range and have been based on a single measure, the ADI-R, which is designed to identify the presence/absence of symptoms rather than to quantify symptom severity.

Objectives: To confirm the factor structure of RRB in a large sample of preschool children with ASD, using the Repetitive Behavior Scale-Revised (RBS-R), an instrument specifically designed to measure this domain; and to examine trajectories and correlates of the resulting factors over a 12-month period.

Methods: The RBS-R was completed by parents of newly-diagnosed 2-to-5-year olds with ASD, participating in a Canadian longitudinal study (Pathways in ASD). Our sample consisted of 283 children (241 males; mean CA=39.5 months; mean MA=22.9 months; 71.7% Caucasian). Exploratory and confirmatory factor analyses were conducted to examine the structure of the RBS-R in this sample. Semi-parametric modeling was used to examine trajectories of the resulting factors over a 12-month period. Spearman's rank order correlations were calculated to examine relationships between the derived factors and adaptive behavior, cognitive functioning, and other ASD symptoms.

Results: A three-factor solution explaining 40% of the variance was selected, using scree plot and goodness-of-fit criteria. The three factors were: Compulsive Ritualistic Sameness Behaviour (CRSB), Self Injurious Behaviour (SIB), and Stereotyped Restricted Behaviour (SRB). Two distinct flat trajectories were found for the total RBS-R score and the CRSB factors, one with higher scores and the other with lower scores. Children with higher CRSB scores were significantly older (r=.19), showed more severe ASD symptoms in the communication and social domains of the ADI-R (r= .61), and had poorer adaptive behavior (Vineland II composite score, r=-.18). Two distinct trajectories were also found for the SIB factor, one of which consisted of a small group of children whose risk for serious SIB persisted across a 12-month period. Children with higher SIB scores were younger (r=-.15) and had lower cognitive ability (Merrill-Palmer-Revised, r=-.16). Finally, we found three groups for the SRB factor, with the highest and lowest trajectories declining over time and the middle trajectory remaining flat. Children with high scores on SRB were younger (r=-.15), had more severe autism (ADI-R, r=.17), and were more impaired on both cognitive (Merrill-Palmer-Revised) and adaptive (Vineland II) skills (r=-.16 to -.21).

Conclusions: Results of the factor analyses confirm the results of studies of RRB in a more homogeneous sample with a different instrument than usually used. The results also indicate that distinct developmental trajectories exist in this independent domain. In general, children with more severe autism, lower cognitive ability, and poorer adaptive behavior had higher rates of RRB across all three factors.

105.122 122 Inventory of Restricted Interests and Repetitive Behaviours in Young Autistic Children: a Questionnaire for Professionals. C. Jacques*, S. Mineau, L. Mottron and C. St-Charles Bernier, *Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*

Background: Stereotyped behaviors and restricted interests in young autistic children are largely documented by parental reports. (Adrien et al. 1993; Dahlgren & Gillberg, 1989; Dawson & Watling, 2000; Gillberg et al. 1990; Lord et al., 1993; Lord, 1995; Moore & Goodson, 2003; Rogers et al., 2003). However, little is known about the psychophysical properties of the objects triggering these behaviors (Ozonoff et al., 2008), although there is a consensus that they are associated with sensory stimulation (Lovaas, Newson & Hickman, 1987; Mottron et al., 2007; Reisman, 1993; Rogers et al., 2003).

Objectives: To document stereotyped behaviors and restricted interests in young autistic children and to identify classes of objects associated with these behaviors.

Methods: Using a literature survey in addition to a qualitative inquiry among one series of professionals, we designed a questionnaire composed of questions about the frequency of restricted interests and repetitive behaviours (RIRB: 36 items), sensory stimulation components (7 items), and other miscellaneous repetitive behaviors (8 items). This resulted in the following RIRB items: hand flapping and finger flicking close to the body or in front of eyes, hand or finger posturing, spinning of entire body, rocking, toe-walking, jumping, closing or squinting of eyes, putting hands on eyes, putting hands on ears, putting fingers in ears, placing objects on ears, placing objects on cheeks, putting fingers or hands in ears or mouth, putting others parts of the body in mouth, putting objects in mouth, putting finger in nose, touching a part of the body repetitively, rubbing hands or fingers on body parts, touching objects, pressing fingers or hands against objects, tapping objects, spinning objects, lining up objects, shaking objects, holding objects in hand, searching to match objects in surroundings, talking about the same subject, making noises with mouth, repeating a sequence of actions, looking at objects with lateral gaze, staring at objects, putting object in front of eyes, smelling objects or people, and throwing or dropping objects. An open series of psychophysical dimensions classified by modality was also proposed, in order to characterize the properties of objects associated to RIRB. In a second part of the study, this questionnaire was sent to a second series of 100 professionals with a mandate for intervention and/or assessment working with autistic children aged up to and including 5 years.

Results: Preliminary analyses (N=25 professionals) of RIRB relative frequency scores indicate that hand flapping, jumping, spinning objects, lining up objects, lateral gaze, and staring at objects are the most frequent RIRB. Specific visual (rotary and linear movements, reflective components) and auditory (melodies) properties are the most frequent psychophysical properties associated with repetitive movements.

Conclusions: These preliminary findings suggest that a specific series of psychophysical properties is implicated in the generation of autistic repetitive behaviours. Further analyses will investigate the possible relation between these properties and current models of autistic atypical information processing.

105.123 123 The Concordance of Repetitive Behaviors in Multiplex Autism Families. K. Carr*[1], J. Pandey[2], S. Hodgson[1], M. Barton[1], J. Green[1] and D. Fein[1], (1)*University of Connecticut*, (2)*Children's Hospital of Philadelphia*

Background: Repetitive and restricted behaviors (RRBs) have received comparatively little attention in the study of children with autism. Furthermore, relatively few researchers have considered RRBs in families with more than one child affected by autism ("multiplex families"). Previous studies of RRBs in multiplex families using the Autism Diagnostic Interview (ADI) have indicated that multiplex siblings tend to be more similar to each other in areas such as circumscribed interests, preoccupations with part-objects, and inflexible language and behavior than are unrelated children (Kolevzon et al., 2004; Georgiades et al., 2007). No known studies of RRBs in multiplex families have used the more detailed Repetitive Behavior Scale – Revised (RBS-R; Bodfish et al., 1999) to assess RRBs. Use of the RBS-R may reveal more detailed information on the concordance of specific RRBs within multiplex families. Objectives: To investigate the familiality of restricted and repetitive behaviors in multiplex autism sibling pairs using the RBS-R. Methods: Thirty-eight pairs of multiplex siblings affected by an autism spectrum disorder (ASD) were evaluated as part of a larger study on the early detection of autism in toddlers. Pairs consisted of non-twin siblings only. The younger siblings of children already diagnosed with an ASD were ascertained on the basis of screening positive on the Modified Checklist for Autism in Toddlers (M-CHAT). Their older siblings were evaluated to confirm their previous diagnoses. Evaluations included a battery of diagnostic, cognitive, and adaptive tests. Diagnoses were assigned based on the DSM-IV symptom checklist, completed using information from testing and clinical judgment. All children in this sample received a diagnosis of Autistic Disorder, Pervasive Developmental Disorder – Not Otherwise Specified (PDD-NOS), or Asperger's Disorder. Parents completed the RBS-R for both children in the sibling pair. The RBS-R consists of

43 items (scored on a Likert scale) across six subscales: Stereotyped Behavior, Self-Injurious Behavior, Compulsive Behavior, Ritualistic Behavior, Sameness Behavior, and Restricted Behavior. Results: Intraclass correlations (ICCs) conducted between older and younger siblings in a pair indicate that multiplex siblings were more similar to each other on several domains of RRB than were unrelated children. Significantly large ICCs between related siblings were found for all subscales except for the Ritualistic Behavior and Restricted Behavior subscales. Conclusions: Analysis of multiplex siblings' scores on the RBS-R indicates that related siblings were more similar to each other in several RRB areas compared with children who are unrelated. Previous studies have found multiplex siblings to be more similar to each other than to unrelated children on behaviors such as preoccupation with part-objects. These results did not replicate this finding, as the ICC for the RBS-R's Restricted Behavior subscale (which included items related to preoccupation with part-objects) was not significant. Other previous findings were replicated, however, including the familiality of inflexible behavior (the RBS-R's Sameness Subscale). These preliminary results suggest that prior research assessing RRBs with the ADI may not have fully described the familiality of RRBs given the limited range of the ADI's RRB questions.

105.124 124 Ritualistic and Adaptive Behaviors in Children with and without Autism Spectrum Disorders. C. S. Ghilain* and D. W. Evans, *Bucknell University*

Background: In contrast to the widespread attention given to the social and communication deficits associated with autism spectrum disorders (ASD), little work has addressed the repetitive and ritualistic behaviors associated with autism. Less work has examined the adaptive and maladaptive correlates of repetitive behaviors in ASD.

Objectives: This pilot study focused on the ritualistic and repetitive behaviors exhibited by children with and without autism, and identifies adaptive and maladaptive correlates of these behaviors. We examined the continuities and discontinuities between normative rituals and routines observed in typically developing children and those with ASD.

Methods: Parent report measures (Childhood Routines Inventory (CRI), Child Behavior Checklist (CBCL), Adaptive Behavioral Assessment Scales (ABAS)) assessed childhood behaviors in 10 children with autism (mean CA 15 years, mean MA=6.8) and a mental-aged matched, typically developing comparison group (n=10; mean CA 7.2 years, mean MA=6.1). The CRI measures normative compulsive-like behaviors, including "Just Right" (e.g., sensitivity to imperfections in toy/clothes) and Repetitive Behaviors. The CBCL measures internalizing and externalizing problem behavior, and the ABAS measures adaptive behavior.

Results: Oneway ANOVA revealed significant differences between the two groups of children on all measures. The ASD and typical groups differed on all three subscales of the CRI: Mean Just Right subscale, Mean Repetitive Behavior subscale, and Mean CRI scale ($p < .05$). For all analyses the children with ASD were reported to engage in greater frequency/intensity than the typically developing children. As expected, the children with ASD exhibited more symptoms as measured by the CBCL than the comparison group. Differences emerged on Withdrawal, Social Problems, Thought Problems, Attention Problems, and Total Problems.

Next, we explored how adaptive and maladaptive behaviors serve as predictors of compulsive-like behaviors measured by the CRI, and whether adaptive/maladaptive behaviors differentially predict compulsive-like behavior for children with and without ASD.

A series of stepwise regressions were performed with CBCL internalizing and externalizing factors entered as predictor variables for each CRI subscale. Externalizing Problems predicted 48% of the variance in repetitive behaviors in children with autism.

Each CRI scale was entered as the criterion variable with the ABAS subscales (ABAS Practical Composite, General Adaptive Composite Scores, Conceptual Composite Scores, Social Composite Scores) serving as predictor variables. For the ASD group, ABAS Practical Composite Score was a significant (and negative) predictor of CRI Repetitive Behavior ($p<.01$), accounting for 62.7% of the variance. The ABAS Practical Composite Score predicted Mean CRI, (41% of the variance, again negative). None of the adaptive/maladaptive variables predicted

accounted for significant variance in the CRI for the typically developing children.

Conclusions: Though typically developing children engage in ritualistic behaviors in early childhood, when matched on developmental level, children with autism engage in more compulsive-like behaviors. Also, compulsive-like behaviors may serve different functions for children with and without autism. For children with ASD, externalizing behaviors predict compulsive-like behaviors, whereas for typically developing children, compulsive-like behaviors may not signify maladaptation – a hypothesis forwarded in previous work. Future research is called for to elucidate the nature of compulsive-like behavior in children with and without ASD.

105.125 125 Sex Differences in Repetitive Sterotyped Behaviors in Autism: Multiplex Versus Singleton Families. R. K. Abramson*[1], A. V. Hall[2], S. Ravan[1], M. L. Cuccaro[3], J. R. Gilbert[3], M. A. Pericak-Vance[3] and H. H. Wright[1], (1)*University of South Carolina School of Medicine*, (2)*Univ. S. Carolina Sch. Public Health*, (3)*University of Miami Miller School of Medicine*

Background: Szatmari et al (2008) examined sex differences in repetitive stereotyped behaviors (RSBs) from the ADI-R in autism spectrum disorders (ASDs) of multiplex families. Families were grouped by those with affected sibs who were male only (MO), female only (FO), and male from male/female (FC) probands and females from male/female (FC) probands. He found that (1) the RSB scores across the 4 gender groups were significantly different (2), females had lower RSB scores than males, (3) the largest RSB difference was between males and females from FC families and (4) males from FC families had significantly higher RSB scores than males from MO families. He concluded that these gender differences in RSB in ASD families support a gender specific model of genetic liability in ASD. He did not report on RSB scores in singleton families. This study replicates his multiplex model in our data set. In addition, it evaluates RSB scores for females in singleton families versus males in singleton families.

Objectives: To evaluate the effect of gender and level of speech on RSB scores in male and females in multiplex, as well as, singleton families.

Methods: The RSB total scores for 236 children with an ADI-R diagnosis of an ASD were used in the analysis. For the multiplex families, a generalized linear model was used to evaluate the effects of gender with level of speech as a covariate on the RBS total scores for males in MO (n=46), females in FO (n=13), males in FC (n=19) and females from FC (n=19). For singleton families a generalized linear model was used to evaluate the effects of gender (male, n=202; female, n=34) with level of speech as a covariate on the RBS total scores for males and for females.

Results: The RSB scores across the 4 gender groups were significantly different $X_{(3,92)}$=13.079, p=0.004. Females had lower RSB scores than males. Male MO were significantly higher than female FO, p=0.046 and female FC, p=0.002. Female FC were significantly lower from male FC, p=0.005. Male FC had the highest RSB scores, but in this small sample they were not different than male MO scores. Overall, female FO had the lowest RSB scores. The RSB scores for males in singleton families did not differ from females, p=0.352.

Conclusions: This study supports the Szatmari study that suggests a gender specific model of genetic liability in multiplex families in ASD. Given the much smaller sample size in this study, to confirm the findings of Szatmari speaks to the significance of this difference. There was no difference between male and female RSB scores in the 236 singleton families. Further study is needed to conclusively answer the question: Do singleton families represent a different genetic liability group?

105.126 126 Behavioral Measure of Reward for Restricted Interests in Autism Spectrum Disorder. S. M. Bolton*[1], A. A. Cosby[1], C. P. Burnette[2], J. H. Foss-Feig[3] and C. Cascio[4], (1)*Vanderbilt School of Medicine/Kennedy Center for Research on Human Development*, (2)*Vanderbilt School of Medicine*, (3)*Vanderbilt University*, (4)*Vanderbilt University School of Medicine*

Background: Autism spectrum disorders are complex, behaviorally-defined developmental disorders whose diagnosis by DSM IV-TR (2000) criteria requires clear evidence of dysfunction in three domains: social relatedness, communication, and restricted or repetitive behavior. The third domain may manifest in a variety of ways, one of which is a tendency for intense, circumscribed interests that may be pursued to a degree that interferes with daily life. So compelling are these interests for children with autism that they are often used in the classroom

as motivational tools, suggesting that they are highly rewarding. Objectives: The goal of this study was to quantify the reward value of images related to these restricted interests by allowing participants to control the display duration of images either related or unrelated to their specific interest. Methods: Two groups, autism and control, were presented with images related or unrelated to their interests while asked to press a button either to increase or decrease the display time for each respective image. There were ten children in each group, ranging in age from eight to seventeen years of age. An inclusion criterion for controls was the presence of a strong hobby or interest. The parents of children in both groups were interviewed using the Yale Special Interests Interview (YSII) (South et al., 1999) to assess and score the severity of interference to the subject's own functioning in daily life due to the restricted interests/interests. Results: We found that the autism group's button presses resulted in longer display times for their own interests compared to controls' presses for their own interests. There was no significant difference in display time between the groups when presented with unrelated images. We also found a positive correlation between interference in daily life as measured by the YSII and the time of the restricted interest displayed. Conclusions: Individuals with autism will often work and make extreme efforts to gain access to objects, activities, or media related to their restricted interests to the detriment of other behaviors. The possibility of a relationship between the extent of the rewarding nature of restricted interests and the detriment to daily social activities is supported in this study. Expansion of this behavioral study using fMRI is currently underway in our laboratory to determine whether brain reward circuitry is involved when viewing images related to restricted interests in autism.

105.127 127 Relationship Between Social Severity and Sensory Processing in Children with High Functioning Autism Spectrum Disorders. C. Hilton*[1], P. D. LaVesser[1], J. Harper[2] and A. Abbacchi[3], (1)*Washington University*, (2)*Saint Louis University*, (3)*Washington University School of Medicine*

Background: Although diagnostic criteria for autism does not include sensory processing deficits, literature describes many sensory processing abnormalities for these children. Researchers have identified modulation difficulties including both hyposensitivities and hypersensitivities to a variety of sensory stimuli in children with autism (Dunn, Smith Myles, & Orr, 2002; Liss, Saulnier, Fein, & Kinsbourne, 2006; Myles et al., 2004).

Objectives: This study examined the relationship between social severity and sensory processing in children with high functioning autism spectrum disorders (HFASD).

Methods: Study methods were in compliance with the guiding policies and principles for experimental procedures endorsed by the National Institute of Health. A linear regression design was used to compare the scores between a social severity assessment and a sensory processing assessment of children with HFASD. Children with HFASD (N = 36), and a control group (N = 26), ages 6 to 10, participated in the study. The participants were full-term, had an overall reported IQ of at least 70, and had no history of cerebral palsy, or any other diagnosed major neurological condition.

The Social Responsiveness Scale (SRS, Constantino & Gruber, 2005), a quantitative trait measure of autistic social impairment was collected from the parent perspective and used to assess social severity. The Sensory Profile (SP, Dunn, 1999), a 125-item questionnaire that describes responses to sensory events in daily life and measures the degree to which children exhibit problems in sensory processing, modulation, behavioral and emotional responses and responsiveness to sensory events, was used to assess sensory processing.

Results: Definitely atypical responses in at least one sensory system (auditory, visual, vestibular, touch, multisensory, and oral sensory) were seen in 100% of the severe HFASD subjects, 60% of the mild to moderate, and 23% of the typical subjects. Definitely atypical responses in at least three of the six sensory systems were seen in 63% of severe, 30% of mild to moderate, and none of the typical subjects. Moderate to strong correlations were found between the SRS scores and each of the six sensory system scores. Regression analysis indicated a significant predictive relationship between the six sensory system scores and the SRS raw scores, with an R square value of .709, with multisensory processing and touch processing having the strongest predictive relationship to the SRS raw scores.

Conclusions: The relationship between the SP sensory system scores and the SRS scores

indicates that auditory, visual, vestibular, touch, multisensory, and oral sensory processing are related to autism severity and have significant importance for understanding the neurobiology of autism.

105.128 128 Cognitive Profiles and Restricted and Repetitive Behaviors: An Early Analysis of Data from the Autism Center of Excellence and Simons Simplex Collection Studies at UIC. R. Loftin*, C. W. Brune, S. J. Guter and E. H. Cook, *University of Illinois at Chicago*

Background: A wide range of cognitive functioning exists among children with autism spectrum disorders (ASDs). Intelligence quotients (IQs) for individuals with ASDs range from the immeasurably low to immeasurably high. Unusual splits in cognitive ability are common. For example, relative, and often normative, strengths in verbal ability occur alongside visual-spatial processing deficits with high frequency in certain individuals with ASD (Williams, Goldstein, Kojkowski, & Minshew, 2008), while strength in visual processing and relative deficit in verbal processing are also commonly observed (Happé, 1994). The heterogeneity in presentation of restricted and repetitive behaviors (RRBs) is also well documented in this population (Lewis & Bodfish, 1998).

The relationship between cognitive functioning and RRBs is not yet entirely clear, however. Individuals with intellectual disabilities and ASDs have a higher rate of repetitive motor mannerisms than individuals with ASDs and no cognitive deficit, as well as children with intellectual deficits alone (Szatmari et al., 1989). However, we know less about the relationship of cognitive functioning to other categories of RRBs, such as resistance to change and circumscribed interests. In particular, we have yet to examine the relationship between unusual cognitive profiles, such as highly significant differences between verbal and nonverbal ability, and RRBs.

Objectives: Broadly, this study will explore the relationship between cognitive profiles and RRBs in individuals with ASDs. In particular, whether three factors of RRBs (motor mannerisms, insistence on sameness and circumscribed interests) (Cuccaro et al, 2003; Lam, Bodfish, & Piven, 2008) occur at different rates relative to cognitive functioning, in particular among individuals with significant VIQ/NVIQ splits (i.e., a difference of more than 1.5 standard deviations).

Methods: Participants will include approximately 120individuals, ages 3-28years, participating in genetic studies of autism with a clinical diagnosis of an ASD based on the Autism Diagnostic Interview-Revised (ADI-R), Autism Diagnostic Observation Schedule (ADOS), and DSM-IV. Measures of cognitive functioning were chosen based on the participants' age and language level, and included the DAS-II, WISC-IV, and WASI. The subscales from the Repetitive Behavior Scale-Revised (RBS-R) will be used as a measure of severity of current RRBs. The three RRB FACTORS derived from the ADI-R will also be used to provide measures of past RRB. The current factors will also be derived for comparison on the same measure. Correlations between RRB scores, and IQ scores (verbal, non-verbal, overall) will be calculated. Patterns of RRB and cognitive functioning will be explored by comparing the mean and variance of RRB scores. Patterns of RRBs for individuals whose VIQ differ by more than 1.5 standard deviations from their NVIQ will be further examined.

Results: Results of the data analysis described above will be presented.

Conclusions: These results will suggest whether different profiles of RRBs emerge among individuals with significant splits in cognitive ability in this relatively diverse sample of individuals with ASD.

105.129 129 Tactile and Auditory Hypersensitivity in Individuals with Autism Spectrum Conditions. T. Tavassoli*[1], E. Ashwin[1], C. Ashwin[1], B. Chakrabarti[2] and S. Baron-Cohen[3], (1)*Autism Research Centre, University of Cambridge*, (2)*University of Cambridge, Autism Research Centre*, (3)*University of Cambridge*

Background: Anecdotal reports suggest sensory differences in autism spectrum conditions (ASC). In addition, studies using questionnaires such as the Sensory Profile have revealed sensory abnormalities in over 90% of children with ASC.

Objectives: This study explores sensory sensitivity using detection tasks in both touch and hearing in female and male adults with and without ASC. We aim to test: (1) if adults with ASC show hyper-sensitivity in both auditory and tactile modalities; (2) if such hypersensitivity is correlated across modalities.

Methods: 20 adults (8 females, 12 males) with a prior diagnosis of ASC were matched to 20 adult

controls (8 females, 12 males) on age, sex and IQ. The Semmes Weinstein Von Frey Aesthesiometer for Touch Assessment, and the Audio-CD for auditory threshold measurement were used to measure tactile and auditory sensitivity respectively. The Autism Spectrum Quotient (AQ) was used to measure autistic traits.

Results: The ASC group was significantly more sensitive to tactile stimulation than the control group ($U = 99.5$, $p < 0.005$). The effect size was large (Cohen's $d=3.9$, $r= 0.89$) The ASC group also showed significantly higher auditory sensitivity at high frequencies (above 16K Hz) ($F=6.43$, $p=0.015$). Tactile and auditory sensitivity were positively correlated for both ASC and controls (Spearman's rho = .453, p = .004).

Conclusions: This study confirms hypersensitivity to touch and hearing at high frequencies in the same individuals with and without ASC, and that sensitivity in both modalities is correlated with each other. These findings suggest that hypersensitivity may be a core feature of the ASC phenotype. This has implications for the design of ASC-friendly sensory environments, diagnostic tools and for future genetic research.

105.130 130 Assessments of Stimulus Modulation in Autism. M. Tommerdahl*[1], E. Francisco[1], J. Holden[1], Z. Zhang[1] and G. T. Baranek[2], (1)*University of North Carolina*, (2)*University of North Carolina at Chapel Hill*

Background:

Adults with autism exhibit inhibitory deficits that are often manifested in behavioral excesses, such as repetitive behaviors, and/or sensory hyper-responsiveness. If such behaviors are the result of a generalized deficiency in inhibitory neurotransmission, then it stands to reason that deficits involving localized cortical-cortical interactions – such as in sensory discrimination tasks – could be detected and quantified.

Objectives:

This study exemplifies a newly developed method for quantifying sensory testing metrics. Our novel sensory discrimination tests may provide (a) an effective means for biobehavioral assessment of deficits specific to autism and (b) an efficient and sensitive measure of change following treatment.

Methods:

The sensory discriminative capacity of subjects with autism (n=12, age range 16-40) and age matched controls (n=50) was compared for assessing the relationships between two nonstationary vibrotactile stimuli delivered to the glabrous skin. In one protocol, the intensity of the two stimuli were initially the same but were diverted at different rates and subjects assessed which of the two stimuli were more intense. In a second protocol, the intensity of the two stimuli were initially very different, but were modulated until they were equal, and subjects indicated when the stimuli were first perceived to be equal. A third protocol was used to obtain observations of the differences between static and dynamically modulated vibrotactile thresholds in each of the subjects.

Results:

Although the duration of modulation of the stimuli had a pronounced effect on the ability of the control subjects to either differentiate or match the stimuli, there was less of an effect on the observations obtained from the autism subjects. However, comparison of the vibrotactile thresholds obtained using static vs. modulated stimuli revealed that the modulation of the stimulus had a much more pronounced impact on the thresholds of the autism group.

Conclusions:

The reduced impact of the duration of the modulated vibrotactile stimuli and the increased impact of the rate of change of the modulated vibrotactile stimuli on the responses of the subjects with autism was interpreted to be consistent with the reduced GABAergic mediated inhibition described in previous reports. One significant aspect of this study is that the methods could prove to be a useful and efficient way to detect specific neural deficits in autism and perhaps monitor the efficacy of pharmacological or behavioral treatments.

105.131 131 The McGurk Effect in Children with ASD: Examining Unisensory and Multisensory Responses to Speech Cues. J. H. Foss-Feig*[1], L. E. Dowell[1], C. P. Burnette[2], C. Cascio[3], H. Kadivar[1], M. T. Wallace[1] and W. Stone[1], (1)*Vanderbilt University*, (2)*Vanderbilt School of Medicine*, (3)*Vanderbilt University School of Medicine*

Background: The ability to synthesize information across sensory modalities into unique multisensory percepts is necessary for

understanding the world's complexities, including for understanding speech. In children with ASD, several studies have shown reduced susceptibility to the McGurk effect, a multisensory speech illusion; some have also shown deficits in lip-reading, the unimodal (i.e., visual) speech cue. According to the principle of inverse effectiveness, when unisensory stimuli are weak in eliciting responses, they are likely to induce increased multisensory responsiveness in combination with other spatially/temporally proximal sensory inputs. One would expect that, if lip-reading skills are deficient in ASD, enhanced integration of the auditory speech signal would occur. It is important to understand the interplay between unisensory and multisensory speech perception to clarify the nature of (multi)sensory deficits that may impact conversational and social interchanges for individuals with ASD.

Objectives: To examine the accuracy with which children with ASD perceive auditory and visual speech input, as well as explore multisensory integration of audiovisual speech cues using the McGurk effect.
Methods: This study included 16 children with ASD and 17 children with typical development (TD), 8-17 years of age. Children with ASD and TD did not differ on age (ASD: mean=12.6yrs; TD: mean=12.1yrs), gender (ASD: 81.3%male; TD: 82.4%male), or IQ (ASD: mean=108.5; TD: mean=107.3), (all ps>0.50). Children with ASD were administered the ADOS and parents were administered the ADI-R to confirm diagnoses; all met cutoff thresholds on both instruments. Participants completed a McGurk task; on audio-visual trials, auditory presentation of the syllable "ba" fused with visual input of a woman mouthing the syllable "ga" typically produces an illusory percept of "da" or "tha". Unisensory visual trials (i.e., no sound, woman mouthing "ga"), as well as auditory trials (i.e., still face, sound clip of "ba") were also presented. Participants indicated perceived syllables via button-press response. Group comparisons were conducted comparing the percent of trials on which auditory-visual fusion (i.e., perceiving "da"/"tha") was reported on auditory-visual trials and comparing perceptual accuracy on auditory- and visual-alone conditions.

Results: No group differences were found on perceptual accuracy for auditory-alone trials, t(31)=-1.158; p=.26. Children with ASD were 65.3% (SD=31.2) accurate, while children with TD were 77.8% (SD=30.3) accurate. Children with ASD were less accurate (27.6%; SD=19.2) than children with TD (45.4%; SD=22.2) on visual-alone (i.e., lip-reading) trials, t(31)=-2.435; p=.02. No group differences were observed in susceptibility to the McGurk effect (ASD: 28.9%, SD=35.0; TD: 29.5%, SD=28.8), indexed by report of fusion syllables "tha" and/or "da", t(31)=-.548; p=.59.

Conclusions: This study found deficits in lip reading abilities in children with ASD, but no differences in auditory speech perception or in susceptibility to the McGurk effect. These findings suggest intact multisensory integration in response to speech stimuli in children with ASD, for whom the visual speech cue is difficult to perceive alone. Results are in keeping with other findings of intact audio-visual integration of simple, non-speech stimuli. Therefore, future studies should explore multisensory integration across stimulus complexity levels to clarify the nature of multisensory deficits in ASD.

105.132 132 Discrimination of Visual Motion in Autism Is Normal When Response Times Are Controlled. K. von Bochmann*, N. Dill and R. J. Krauzlis, *Salk Institute for Biological Studies*

Background: Individuals with autism spectrum disorder (ASD) exhibit unusual performance in visual motion discrimination tasks. It is not clear whether the observed impairments are attributable to abnormalities in the early stages of visual processing or in later stages related to attention or decision-making. Hypothesizing that they are due to the latter, we measured reaction times and choices of 6 ASD-diagnosed and 7 typically developing adolescents in a 2AFC motion discrimination task. In this "self-paced" task, subjects fixated a central spot, presented together with a stochastic motion patch (8º diameter, centered 8º above fixation) of 250 ms and two response dots placed 8º to the left and right of the fixation spot. The direction of motion was equally likely to be rightward or leftward, and the strength of motion was randomly selected from 9 values between 0 and 40% coherence. Subjects were asked to fixate the central spot until they could judge the direction of motion, and to indicate their choice by moving their eyes to the response dot in the same direction as the judged motion. Subjects received auditory feedback about their choice after each trial. We measured saccades on each trial to examine the subjects' reaction times as well as their choices. We found

that in comparison to control subjects, ASD-diagnosed subjects had higher thresholds for discriminating the direction of visual motion. In addition, their reaction times were shorter than those of control subjects. Moreover, in contrast to control subjects, the reaction times of ASD-diagnosed subjects did not vary with the strength of the motion signal. This suggests that ASD-diagnosed subjects may perform worse in motion discrimination tasks because of abnormal temporal control of the decision processes guiding the perceptual choice or controlling the behavioral response.
Objectives: To further investigate the role of temporal control in these effects on visual discrimination, we designed a "delayed-response" version of the task that controlled how long the subjects viewed the visual motion stimulus before giving their answer.

Methods: In this version of the task, subjects were instructed to maintain fixation on the central spot until the two response dots appeared (750 ms). The onset of the response dots indicated to the subjects that they should indicate their choice, in the same way as in the previous experiment.
Results: The ASD-diagnosed subjects performed better in discriminating the direction of visual motion in the "delayed-response" task (thresholds between 7 and 29%, 15% mean) than in the "self-paced" task (thresholds between 13 and 32%, 22% mean). Delaying the response time resulted in ASD-diagnosed subjects performing similarly to control subjects (thresholds between 9 and 28%, 16% mean).
Conclusions: These findings challenge the idea that the observed impairments in motion processing of ASD-diagnosed individuals are due to abnormalities in the early stages of visual processing, and instead suggest that the impairment is related to abnormalities in the temporal control of the decision process underlying the behavioral response.

105.134 134 Visual Processing Ability Predicts Facial Affect Comprehension in Children with Autism Spectrum Disorders. C. Demopoulos*, M. Stepansky and J. D. Lewine, *Alexian Brothers Medical Center*

Background: The research on facial affect comprehension in individuals with Autism Spectrum Disorders (ASD) varies in both methodology and outcome. Different stimulus, participant, and design characteristics across studies make it difficult to draw definitive conclusions, but the current state of the literature suggests that the sources of these deficits are diverse and complex. The heterogeneity of symptom presentation within the autism spectrum population adds to the convolution. Explanations for the inconsistent presence of deficient facial affect processing in ASD have been offered, including age of participants, visual sensory/perceptual differences, and social relevance of face stimuli. Studies that have incorporated nonsocial visual control tasks in their examination of face and facial emotion perception have inconsistently found perceptual impairments in groups with poor affect recognition. The majority of these studies have examined group averages, which can mask individual variation in both visual perception and affect recognition. Few studies, however, have examined the relationship of these perceptual deficits to facial affect processing directly.

Objectives: This study examined the relative contributions of general visual processing ability, visual encoding of faces, and participant age to the prediction of facial affect comprehension in children with ASD.

Methods: General visual processing ability was assessed by the matching subtest of the Wide Range Assessment of Visual Motor Ability (WRAVMA). Ability to visually encode faces was estimated by the immediate recognition score of the memory for faces subtest of the Children's Memory Scale (CMS). Facial affect comprehension was measured by the child and adult faces subtests of the Diagnostic Assessment of Nonverbal Accuracy (DANVA-II). Participants were 64 male and 7 female children ages 5-18 years (m = 10.68; SD = 3.9) undergoing neuropsychological assessment in a pediatric neuropsychology clinic. Analyses were planned to examine group differences relative to the standardization sample as well as symptom-level relationships within this ASD group. One-sample t-tests against the normative means were performed on the WRAVMA, CMS, and DANVA-II measures. Regression analyses were performed to examine the relative contribution of participant age, facial encoding ability, and general visual processing performance to the prediction of facial affect comprehension.

Results: While scores on the CMS ($t(70) = -8.24$, $p<.001$) and DANVA-II tasks (adult faces $t(70) = -3.09$, $p = .003$; child faces $t(70) = -5.56$, p

<.001) were significantly below the mean of the standardization samples, only the mean of the CMS task approached clinical significance (absolute Z-score > 1.0). The linear combination of predictors accounted for a significant amount of variability in affect comprehension for both adult (R^2 = .26, R^2_{adj} = .22, F(2,68) = 7.71, p<.001) and child faces(R^2 = .17, R^2_{adj} = .13, F(2,68) = 4.47, p=.006). Only the partial correlations between the general visual processing task and the affect comprehension tasks were significant.

Conclusions: While ASD group scores were not impaired in visual processing ability, regression analyses revealed that visual processing accounted for a significant proportion of the variance in facial affect comprehension. Results highlight the need for symptom-level analyses in ASD research with relevant comparison groups.

105.135 135 Children with Autism Spectrum Disorders and the Rubber Hand Illusion: Evidence of Decreased Multisensory Integration. C. Cascio*[1], A. A. Cosby[2], C. P. Burnette[2], J. H. Foss-Feig[3] and S. M. Bolton[4], (1)*Vanderbilt University School of Medicine*, (2)*Vanderbilt School of Medicine*, (3)*Vanderbilt University*, (4)*Vanderbilt School of Medicine/Kennedy Center for Research on Human Development*

Background:

Children with autism spectrum disorders (ASD) experience sensory and perceptual events differently than typically developing (TD) children. One presumed source of altered perceptual experience is aberrant integration of information from multiple sensory modalities. In the rubber hand illusion, simultaneous visual and tactile input converge to modify perception in a third modality, proprioception. We hypothesized that children with ASD would differ from controls in their susceptibility to this illusion.

Objectives: To examine multisensory integration of visual and tactile input in ASD using the rubber hand illusion.
Methods: Thirteen children with ASD and thirteen children with TD, ages 8-17, were tested on the rubber hand paradigm. The groups were matched for age, IQ, gender, and handedness. ASD diagnosis was confirmed with the Autism Diagnostic Interview - Revised (ADI-R), Autism Diagnostic Observation Schedule (ADOS), and the judgment of a licensed clinical psychologist. In the experimental condition, the experimenter used a soft brush to synchronously stroke a visible rubber hand and the child's own hand, which was hidden from view. In the control condition, the strokes to the real and rubber hands were delivered asynchronously. Before and after each condition, the child was asked to make a judgment about the position of his/her obscured hand. The dependent variable was the drift of perceived position relative to the position of the visible rubber hand, and was assessed using one sample t-tests.
Results: In the control condition (asynchronous brushing), neither group exhibited significant drift toward the rubber hand. In the experimental condition (synchronous brushing), the control group showed a significant drift in the direction of the rubber hand, while the autism group did not. The amount of drift in the autism group was negatively correlated with spontaneous imitation during development as rated on the ADI-R.
Conclusions: The rubber hand illusion depends on the integration of visual and tactile input to influence proprioception. Unlike the control group, children with ASD did not show a significant influence of this integrated multisensory input on proprioception, suggesting decreased integration of visual and tactile input. Additionally, a trend for an association between the development of imitation skills and the strength of the illusion was noted in the ASD group. The rubber hand illusion activates premotor cortex, a site that is part of the mirror neuron system, which has been implicated in autism and is thought to be important for developing imitation skills. The link between the illusion and imitation skills may reflect a contribution of this system to multisensory integration deficits in ASD.

105.136 136 Sensory Profiles and Bisensory Facilitation: Is Unimodal Processing Impaired, but Audio-Visual Integration Intact in ASD?. C. R. Stewart*[1], S. Sanchez[1], E. L. Grenesko[1], A. J. Lincoln[2] and R. A. Mueller[1], (1)*San Diego State University*, (2)*Alliant International University*

Background:

Atypical responses to sensory stimuli are frequently seen in children with autism spectrum disorders (ASD), implying that sensory information may be processed abnormally. In previous studies, Dunn's (1997) Sensory Profile scores have been found to differ between children with autism and their typically developing (TD) peers (Kern et al., 2007). It has been further suggested that individuals with ASD have difficulty integrating auditory- visual information in verbal conditions (Smith & Bennetto, 2007).

Data on sensory integration in nonverbal tasks are less consistent. We used a nonverbal auditory-visual paradigm, for which bisensory facilitation effects (reduced response times when congruent stimuli are presented in both modalities) have been reported in typical adults.

Objectives:

To examine whether bisensory facilitation is affected in autism and whether facilitation may be related to abnormal sensory processing.

Methods:

Participants were 13 boys (mean age 13.8, sd=2.2) with ASD and 13 TD boys (mean age 14.0, sd=2.3), matched for nonverbal IQ. Participants completed the Adolescent/Adult Sensory Profile questionnaire prior to the experimental task, which included three stimulus types: auditory (a high or low tone), visual (a dot appearing in a top or bottom box that was presented throughout), and bisensory (congruent auditory and visual stimuli). Participant responded by pressing a "high" or "low" button on a button-press device. Stimuli were presented in two different conditions: a Repetitive Task (REPT) consisting of repeated presentation of a given stimulus type in separate runs, and a Modality Switching Task (MST) with randomly alternating stimulus types.

Results:

There was no group difference in RT, $F(1,22)=1.43$, $p=.30$, or accuracy , $F(1,22)=1.75$, $p=.20$. Both groups showed a bisensory facilitation effect, with a decrease in reaction time during the bimodal condition, compared to either unimodal condition, $F(1,22)=56.95$, $p<.01$. For the Sensory Profile, a one-way ANOVA showed that the ASD group had significantly higher scores for the Low Registration quadrant than the TD group, $F=9.98$, $p=.005$. In the ASD group (but not the TD group), scores on this quadrant were significantly correlated with response times for auditory trials of the REPT, $r=.77$, $p=.005$, and for both unimodal and bimodal conditions of the MST (auditory $r=.62$, $p=.02$, visual $r=.57$, $p=.04$, bimodal $r=.62$, $p=.02$) .
Conclusions:

There was no evidence of impaired sensory integration in the ASD group, as both groups showed bisensory facilitation. However, sensory scores were abnormal in our ASD group, consistent with previous studies. Specifically, higher scores on the Low Registration quadrant of the Sensory Profile reflect slowed detection of sensory stimuli (Brown & Dunn, 2002), as supported by our finding of correlation with response times for auditory stimuli and with generally slowed response on the modality switching task, for the ASD group. The pattern of results suggests that low-level sensory impairment is more common and more severe in ASD than any potential defects in sensory integration.

105.137 137 Pilot Study for Measuring Sensitivity to Social Touch in School-Age Children with Autism Spectrum Disorders. M. J. Ackerman*, P. Lewis, A. Klin and W. Jones, *Yale University School of Medicine*

Background: A variety of anomalous sensitivities to touch have been described anecdotally in children with autism spectrum disorders (ASD). Reports of these behaviors cover a wide range of responses, including (but not limited to) undersensitivity to pain, oversensitivity to light touch, preference for deep pressure, and atypical reaction to social touch. Most of these reports have been qualitative, however, and there are few studies with direct, quantitative measurements of sensitivity to touch in individuals with ASD. And to our knowledge, there have been no studies that directly measure sensitivity to social touch in children with ASD.

Objectives: To measure selective sensitivity to contingent social touch in school-age children with autism spectrum disorders in comparison with matched, typically-developing peers. Control conditions will measure sensitivity to mechanical (non-social) touch and sensitivity to non-contingent social touch. We will test the hypothesis that children with ASD exhibit reduced sensitivity to contingent social, but not mechanical, touch.

Methods: We designed and built a novel device for measuring haptic interaction between two individuals or between one individual and a pre-recorded touch signal. The device consists of horizontal rollers, linked remotely, that can be turned by either of two participants. The rollers of each participant are coupled electromechanically, so that if one participant moves a roller, the other participant will feel that movement on his own roller; if both participants move their rollers, the

resulting motion of each roller will be proportional to the force applied to both. The force applied by the test participant in response to varying input signals (contingent social, non-contingent social, and mechanical) is the dependent variable for measuring haptic sensitivity.

Results: Preliminary results demonstrate the utility and effectiveness of the interface for measuring social touch. In pilot development, typical participants report a keen sensation of feeling another person's actions during the contingent social touch condition, and a clear sense of non-social touch during the mechanical touch condition.

Conclusions: Large amounts of previous research with individuals with ASD have documented atypical processing, particularly during social interaction, in the domains of hearing and vision, but the sense of touch has not been closely studied. Typically-developing individuals are highly sensitized to recognize certain kinds of touch as social, and to react and respond in kind. Developing research platforms for the quantification of response to social touch will be an important part of understanding atypical behavioral and neural specialization in individuals with ASD.

105.138 138 Sensory Abnormalities in Twins with ASD: Investigating Associations with IQ and Behavioural Features of ASD. S. Lietz*[1], C. Ames[1], E. Woodcock[1], P. Bolton[2] and F. Happé[1], (1)*Institute of Psychiatry, King's College London*, (2)*Institute of Psychiatry*

Background: Increased rates of sensory abnormalities, such as hypo- and hyper-sensitivity to sound, light, touch, and taste, are consistently reported in studies of individuals with autism spectrum disorders (ASD) (e.g. Leekam et al., 2007, Rogers & Ozonoff, 2005). However, despite a recent increase in studies of sensory abnormalities in autism, it is still unclear why there is such variability in sensory responsivity in individuals with ASD and which behavioural and cognitive aspects of ASD predict high levels of sensory problems. Rogers, Hepburn, and Wehner (2003) examined the occurrence of sensory symptoms in toddlers with autism and other developmental disorders. Significant associations were found in the autism group with the ADOS restricted activities algorithm score, but not with IQ, ADI, or other ADOS scores. In addition to this, the autism group showed more sensory symptoms than the control group. Szatmari et al. (2006) examined the structure of the restricted, repetitive behaviours and interests domain in autism measured by the ADOS and the ADI. Using factor analysis, they found that this domain actually consists of 2 factors: 'insistence on sameness' (IS) and 'repetitive and sensory motor behaviours and interests' (RSMB). High RSMB scores were found to be associated with more autistic symptoms in the social reciprocity domain and lower cognitive functioning. However, their analysis of sibling data to assess familiality of the RSMB factor yielded no significant results.
Objectives: The aim of this study was to investigate potential associations between sensory symptoms, IQ, and other behavioural features of ASD in a sample of teenage twins, as well as to explore the role of genetic factors in contributing to individual differences in sensory abnormalities in ASD, to assess whether sensory sensitivities form part of a broader autism phenotype.
Methods: This study forms part of a large-scale longitudinal twin study (TEDS - Twins Early Development Study). Twins with ASD (autism, Asperger Syndrome, atypical autism) were recruited for the Social Relationship Study (SRS). The sample for the present study includes 50 ASD twin pairs (at least one twin with ASD) and 50 control twin pairs, aged 12-14 years. Patterns of sensory abnormalities were assessed using the Short Sensory Profile completed by children and parents. The Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview-Revised (ADI-R) were carried out for each twin to evaluate severity of symptoms. Level of cognitive functioning was determined using the Wechsler Abbreviated Scale of Intelligence (WASI).
Results: Results show higher rates of sensory abnormalities in ASD twins as compared to controls. Furthermore, we find interesting results concerning the associations between the sensory sensitivity scores obtained from the Sensory Profile and the ADOS, ADI, and WASI scores. The twin correlations indicate the contribution of genetic and environmental effects to individual differences in sensory responsivity in individuals with autism.
Conclusions: Sensory abnormalities can be severely debilitating for individuals with autism. Understanding why sensory sensitivities affect some children more than others provides the first step to intervention.

105.139 139 Accessibility of Health Services and Age at Autism Diagnosis. A. E. Kalkbrenner*, J. L. Daniels, C. L. Poole, J. C. Chen and M. Emch, *University of North Carolina*

Background: Early diagnosis of autism is important to the success of early intervention. Yet there is a well-documented delay ranging 2-4 years between a parent's concern and eventual autism diagnosis; some children are missed entirely. The relation between geographic access to health services and the timing of autism diagnosis has not been studied.

Objectives: We evaluated the impact of several health services accessibility factors at birth on the age at autism diagnosis among children with autism.

Methods: We included 8-year-old children who met the standardized criteria for autism used by the Autism and Developmental Disabilities Monitoring Network in North Carolina and had a matching NC birth certificate. This multiple-source, active, records-based surveillance network relies on documented behavioral symptoms in developmental records, from which we obtained the presence of and age at a prior autism diagnosis. Health accessibility exposures were measured as provider density, distance to the nearest provider or facility, and residence within a Health Professional Shortage Area (HPSA). Addresses for primary care physicians serving children, specialist physicians likely to diagnose autism, and psychologists were obtained from a medical and psychologist board licensure database. Other diagnostic facilities included the Division of Treatment and Education of Autistic and related Communication handicapped Children, the Child Development Service Agencies of the Early Intervention Program (CDSA), and NC teaching hospitals. Child and provider addresses were geocoded. Provider density and distances were calculated using geographic information systems. A multivariable Cox survival model was used to estimate hazard ratios (HR) of the age at previous autism diagnosis, adjusting for social and demographic factors from the surveillance record (race and child's cognitive status), birth certificate (maternal education, maternal age, marital status), and census (block group median household income).

Results: Of 220 children with confirmed autism and a matching birth certificate, 51 (23%) had no previous autism diagnosis. The remainder had a mean age of diagnosis of 57 months (standard deviation: 22 months, median: 52 months). Several accessibility factors were associated with earlier autism diagnosis, as indicated by elevated adjusted HRs, including: higher count of specialist physicians within a 20-mile road network radius (HR and 95% confidence interval of 1.6 [1.0, 2.4] comparing 250+ providers to < 75), shorter distance to a CDSA (1.4 [0.8, 2.2] comparing < 5 miles to > 20 miles), shorter distance to a teaching hospital (1.5 [1.0, 2.2] comparing proximity < 5 miles to > 20 miles), and not residing within a HPSA (1.3 [0.7, 2.1]). HRs for accessibility measures and early diagnosis were elevated to a greater degree among children with developmental loss or plateau, with married parents, or living in urban areas.

Conclusions: Better geographic accessibility of health services appears to be associated with an increased likelihood of an earlier age at autism diagnosis. The impact of accessibility was found using several different geographic accessibility measures. Many determinants of accessibility were not measured in this case-only study. Considering the location of health services may be useful in targeting efforts to improve early identification of autism.

105.140 140 Changes in Documented Diagnostic Classifications of Children Identified by an Autism Spectrum Disorder Surveillance System. J. Baio[1], L. D. Wiggins*[2], C. E. Rice[1], O. Devine[2] and K. Van Naarden Braun[2], (1)*National Center on Birth Defects and Developmental Disabilities*, (2)*Centers for Disease Control and Prevention*

Background: Recent years have witnessed a surge of interest in the identification and diagnosis of children with autism spectrum disorders (ASDs). Objectives: This study sought to examine changes in documented diagnostic classifications of children identified by a population-based ASD surveillance system in metropolitan Atlanta, GA.

Methods: Participants were 1023 children who met ASD case criteria in surveillance years 2000, 2002, and 2004; the number of ASD surveillance cases increased each surveillance year. Children were identified as a potential ASD surveillance case by abstraction and review of health and educational records in Atlanta, GA. Trained clinicians applied a standardized coding scheme to determine ASD case status. Clinicians also coded evaluation classifications documented by a community professional.

Results: The odds likelihood of receiving a documented classification of all ASDs was significantly higher in 2004 than in 2000; there was a significant decrease in classifications of Autistic Disorder from 2002 to 2004 accompanied

by comparable increases in descriptions of other ASDs, language delay, and motor delay. Other nonASD classifications remained relatively stable, although Sensory Integration Disorder and other specific delays increased slightly. A majority of ASD surveillance cases had an ASD classification noted in surveillance records. However, a substantial minority had no ASD classification noted in available records.
Conclusions: More children were identified as an ASD surveillance case from 2000-2004; the likelihood of receiving an ASD classification increased during this time. These results suggest that more children are being identified and diagnosed with ASDs over a relatively brief period. Documentation of certain developmental delays also increased during this period, which could represent better understanding that ASDs co-occur with other conditions or more comfort describing symptoms of ASDs rather than diagnosing Autistic Disorder. Many children with documented ASD behaviors did not have a documented ASD classification. Thus, children with ASDs may continue to be under-diagnosed.

105.141 141 The Impact of Urbanicity on Diagnosis and Treatment of ASD. J. E. Farmer*[1], A. R. Marvin[2], C. Anderson[2] and K. Law[2], (1)*University of Missouri*, (2)*Kennedy Krieger Institute*

Background:

Children with autism spectrum disorders (ASD) living in rural areas may experience difficulties accessing health and educational services, most notably access to well-established interventions such as applied behavioral analysis (ABA).

Objectives:

To examine diagnostic patterns, educational opportunities, and access to ABA by urban-rural categories for Missouri children with ASD (age<18) enrolled in a national autism registry (Interactive Autism Network).

Methods:

Using a web-based interface, parents of 351 children (83% male) living in Missouri reported information about their child's diagnosis, education, and treatments. The number of children with complete data regarding diagnosis and education was 251 and regarding treatments was 313. Of these, 56 non-Asperger's children were receiving ABA therapies at enrollment (*M* age = 6.08 years; *SD*= 2.98). Results were analyzed by urbanicity using the 2006 National Center for Health Statistics Urban-Rural Classification Scheme: 61% of children lived in large metro areas (12% large central metro; 49% large fringe metro), 21% in smaller metro areas (9% medium metro; 12% small metro), and 18% in non-metro areas (8% micropolitan; 10% rural). To determine differences across the urban-rural continuum for access to ABA, the number of young children (3-9 years) participating in ABA intervention at the time of enrollment (*n* = 38) was compared to those within the same age range who did not report ABA therapy at enrollment (*n* = 105).

Results:

Although there was no difference in age of first concern, children living in smaller metro/non-metro areas were less likely to be diagnosed before age three than children living in the greater metro areas of St. Louis and Kansas City (29% and 53%, respectively; $p<.001$). They had fewer educational options, with 76% attending public school compared to 53% for those in large metro areas ($p<.01$). Those in large metro areas had access to specialized public and private schools that were not an option for most children living in more rural areas. There was no statistically significant difference between large metro areas and more rural areas in the percentage of children with an aide (47% and 55%, respectively); however, of those children who did have an aide, those living in large metro areas were less likely to have a full-time aide than those living in more rural areas (36% and 64%, respectively; $p<.05$). Children in large central metro areas were less likely to have classroom opportunities for inclusion with typically developing peers than those in less urban areas (63% and 86%, respectively; $p<.01$). Furthermore, young children in smaller metro/non-metro areas were less likely to receive ABA services than those in large metro areas (13% and 35%, respectively; $p<.01$). In the majority of cases, the cost of ABA services was free or minimal (74%) and was funded and/or provided by the public school (48%) or Early Childhood programs (26%).

Conclusions:

Living outside of a large metro area may delay ASD diagnosis and limit access to specialized schools and services, but may promote more

inclusive education. Future research will examine national trends.

106 Update On Strategic Plan for Autism Research

Speaker: T. Insel*National Institutes of Health*

Invited Educational Symposium Program
107 Mouse Models as Translational Tools to Discover Treatments for Autism Spectrum Disorders

Moderators: L. Herzing[1]R. Ring[2](1)*Northwestern University Feinberg School of Medicine*, (2)*Wyeth Research*

Organizers: L. Herzing[1]J. N. Crawley[2](1)*Northwestern University Feinberg School of Medicine*, (2)*National Institute of Mental Health, National Institutes of Health*

Speakers: J. N. Crawley[1]R. Paylor[2]G. Lynch[3]L. F. Parada[4](1)*National Institute of Mental Health, National Institutes of Health*, (2)*Baylor College of Medicine*, (3)*University of California at Irvine*, (4)*University of Texas Southwestern Medical School*

Animal models offer powerful research tools to test the many intriguing hypotheses about the causes of autism spectrum disorders, and to evaluate the efficacy of potential treatments. Mice are a social species, with genes, neuroanatomy, neurophysiology, and neurochemistry similar to humans. This Educational Symposium will present case studies of pharmacological, genetic, and behavioral interventions that improve symptoms in mouse models of autism spectrum disorders. Symposium chairs Laura Herzing, Northwestern University, and Robert Ring, Wyeth Research, will promote interactive discussion throughout the session. Jacqueline Crawley, NIMH, will describe mouse behavioral assays relevant to the three diagnostic criteria for autism, and the ability of juvenile peer intervention to prevent social deficits and of MPEP drug treatments to reverse repetitive behavior in the BTBR T+tf/J mouse model of autism. Richard Paylor, Baylor College of Medicine, will present genetic rescue and mGluR5 antagonist treatment of behavioral traits in the Fmr1 mouse model of Fragile X syndrome. Gary Lynch, University of California Irvine, will discuss electrophysiological and dendritic spine abnormalities in the Fmr1 and BTBR mouse models that implicate the actin filament stabilization pathway in synaptic defects. Luis Parada, University of Texas Southwestern, will demonstrate the ability of the mTOR inhibitor rapamycin to reverse macroencephaly, neuroanatomical abnormalities, seizures, and social deficits in Pten mutant mice. These studies represent just a portion of the increasing wealth of available multidisciplinary assays and heuristic mouse models, which are rapidly moving the field forward in the discovery of efficacious treatments for components of autism spectrum disorders.

107.00 Behavioral Phenotyping Assays for Translational Evaluation of Treatments In Mouse Models of Autism. J. N. Crawley*, *National Institute of Mental Health, National Institutes of Health*

Autism is a major mental illness with a strong genetic component. As candidate genes for autism are identified, mice with targeted mutations of these genes are becoming available. Model organisms offer useful translational tools to test hypotheses about single genes, chromosomal locus deletions, copy number variants, epigenetic mechanisms, neurochemical,electrophysiological, synaptic, and neuroanatomical abnormalities, environmental toxins, diets, immune dysfunctions, and other proposed causes of autism.

The key to translational applications is robust, highly replicable functional assays. We developed mouse behavioral paradigms with conceptual analogies to the three diagnostic symptoms of autism. Abnormalities in reciprocal social interactions are assayed longitudinally across developmental ages during juvenile play, automated adult social approach, and reciprocal social interaction tasks. Communication deficits are quantitated by the emission, detection, and behavioral responses to social auditory and olfactory and cues. Motor stereotypies, repetitive behaviors, insistence on sameness, and narrow restricted interests manifest in mice as stereotyped motor behaviors, repetitive self-grooming, perseveration during the reversal phase of T-maze and Morris water maze spatial habits, and restricted exploration of complex environments. Relevant to the associated symptoms of autism, mouse models are assayed for cognitive deficits, anxiety-like traits, seizures, sleep disruption, and hyperreactivity to sensory stimuli. Comprehensive control parameters including measures of general health, reflexes, sensory and motor abilities, detect artifacts caused by physical and procedural dysfunctions.

Representative data will be presented for BTBR T+tf/J, an inbred strain of mice that displays autism-relevant traits in all three diagnostic domains, and for mice with mutations in putative candidate genes for autism. Strong phenotypes relevant to the diagnostic and associated

symptoms of autism, in targeted gene mutations and inbred strains of mice, offer attractive model systems for treatment discovery. Early preclinical data will be presented on pharmacological and behavioral interventions that reverse autism-relevant behavioral phenotypes in the BTBR mouse model of autism.

107.01 Genetic and Pharmacological Modifications of Autistic-Like Behaviors in Fmr1 KO and Other Mouse Models of ASD. R. Paylor*, *Baylor College of Medicine*

Fragile X syndrome (FXS) results from the loss of expression of the Fragile X mental retardation (FMR1) gene. Individuals affected by FXS experience many behavioral problems, including cognitive impairment, hyperactivity, and social anxiety. In addition from 15-25% of individuals with FXS meet the full criterion for autism spectrum disorder (ASD). A mouse model of Fmr1 deficiency (Fmr1KO) exhibits several similar behavioral phenotypes, including alterations in autistic-like behaviors such as social interactions. Identifying and evaluating targets that modify behavioral responses in the Fmr1 KO mouse therefore should help with the initial development and evaluation of therapies for FXS and ASD. Our lab has used both genetic and pharmacological tools to modify the behavior of Fmr1 KO mice. One strategy we have employed is to over-express human FMRP and determine if we rescue abnormal responses in Fmr1 KO mice. Recently we found that both social behaviors and sensorimotor gating are rescued in Fmr1 KO mice that carry the human FMR1 gene. Recent findings suggest that group 1 mGluR5 receptor function may be overactive in Fmr1 KO mice. We have explored the possibility of reducing mGluR5 signaling using pharmacological treatments and gene knockout mice can alter responses in Fmr1 KO mice. Our findings suggest that modifying mGluR 1/5 receptors can alter the behavior of Fmr1 KO mice suggesting that drugs targeting this receptor system may be useful treatments for FXS and ASD.

107.02 Mechanisms Stabilizing Synaptic Plasticity Are Impaired In Models of Autism Associated Disorders. G. Lynch*, *University of California at Irvine*

Consolidation (stabilization) of long-term potentiation (LTP), and quite possibly memory, requires the rapid reorganization of the sub-synaptic cytoskeleton. This process involves two signaling cascades, one that initiates actin polymerization and a second that stabilizes the newly formed actin filaments. We have begun testing if defects in these processes contribute to synaptic disturbances in rodent models of cognitive, and autism-related, disorders, including the Fmr1-knockout (Fmr1-KO) mouse model of Fragile X Syndrome. Hippocampal slices prepared from Fmr1-KO mice proved to have two synaptic plasticity deficits: 1) a modest elevation in the activity-threshold for inducing LTP expression and 2) a slower than normal rate of LTP consolidation. Actin polymerization within spines in the minutes following LTP induction was not measurably different in Fmr1-KO slices vs wild-type controls (Lauterborn et al, 2007), suggesting that the LTP-consolidation defect involves the actin filament stabilization pathway. In accord with this, we have found that the stabilization of LTP involves the small GTPase Rac and its effector p21-activated kinase (PAK), and partial suppression of PAK is reported to reduce synaptic abnormalities in the Fmr1-KO mouse (Hayashi et al, 2007). We are currently attempting to isolate the defective step(s) in signaling through the Rac>PAK filamentous actin stabilization pathway in the Fmr1-KOs. In parallel, we are evaluating the LTP consolidation problems in the BTBR T+ tf/j inbred strain (MacPherson et al. 2008 and unpublished data) that exhibits behavioral traits associated with autism (Macfarlane et al., 2007) with an interest in the possibility of shared impairments in activity-regulation of the spine actin cytoskeleton in the Fmr1-KO and BTBR strains. In all, it is possible that critical synaptic defects in models of autism-related disorders arise from relatively small disturbances to the specialized cellular machinery normally used to convert recently learned material into long-term memory.

107.03 Mouse Models as Translational Tools to Discover Treatments for Autism Spectrum Disorders: Focus On Rapamycin. J. Zhou[1], C. H. Kwon[2] and L. F. Parada*[3], (1)*University of Texas Southwestern Medical Center*, (2)*Ohio State University*, (3)*University of Texas Southwestern Medical School*

The use of mice as genetic tools to study the molecular basis of brain development and function has grown steadily over recent years. Recent human genetic studies have implicated the PI3 Kinase pathway as an underlying cause of a small subset of autism cases that are related to genetically inherited diseases. Using mutant mouse models, we have shown that modulation of the PI3 Kinase pathway can be an indirect source of synaptic modulation. Moreover, mice lacking PI3 Kinase components in mature neurons exhibit stereotypic behavioral abnormalities reminiscent

of autism. Because this signaling pathway is also implicated in many human cancers, drugs that inhibit this pathway are in development. We have applied such drugs, including the specific mTORC1 inhibitor rapamycin in *Pten* mutant mice, with promising outcomes. It is our hope that continued study of these mice will provide insights into the anatomical and cellular basis of at least a subset of autism spectrum disorders.

Oral Presentations Program
108 Screening

108.00 Screening with the First Year Inventory at 12 Months of Age and Diagnostic Outcomes at Two Years in a High-Risk Sample of "Infant Sibs". G. T. Baranek*[1], L. Zwaigenbaum[2], J. Brian[3], S. E. Bryson[4], E. Crais[1], J. Piven[5], J. S. Reznick[1], W. Roberts[6], I. M. Smith[4], P. Szatmari[7] and L. Watson[1], (1)*University of North Carolina at Chapel Hill*, (2)*University of Alberta*, (3)*Hospital for Sick Children & Bloorview Kids Rehab*, (4)*Dalhousie University/IWK Health Centre*, (5)*University of North Carolina*, (6)*University of Toronto*, (7)*Offord Centre for Child Studies, McMaster University*

Background: Longitudinal studies of infant siblings of children with ASD provide a unique opportunity to determine the validity of infant screening tools in a high-risk sample (Zwaigenbaum et al., 2007). The First Year Inventory (FYI) (Baranek, Watson, Crais & Reznick, 2003) is a parental report measure designed to screen 12-month old infants at-risk for ASD or related DD. Developed from research on early features of ASD, the FYI has 61 items, and taps 8 constructs within two broad domains -- sensory-regulatory & social-communication functions.

Objectives: This study aims to test the validity of the FYI in predicting clinical diagnoses of ASD at age two in a high-risk "infant sibs" sample.

Methods: 111 infant sibs and 37 typically-developing controls were assessed with the FYI at 12 months. The original FYI scoring model (Reznick et al., 2007) was used and outcomes were divided into three risk ranges (high: ≥93%ile; moderate: 80-92%ile; low: <80%ile). A research team including a pediatrician and a clinical psychologist, blind to FYI score, conducted developmental (Mullen,) and diagnostic (ADOS) evaluations to determine clinical diagnoses (DSM-IV) at age 2. Thus far, complete data were available for 77 sibs and 30 controls.

Results: At 12 months of age, infant sibs had significantly elevated FYI raw scores and risk percentiles (M=13.57; 74%ile) relative to controls (M=5.14; 35%ile), [t(146)=4.98, $p<.001$]. Scores of controls were comparable to the normative sample. At 2 years of age, 16 (21%) sibs received an ASD diagnosis, 7 (9%) sibs received a diagnosis of language delay, and 23 (30%) sibs had other concerns, whereas 31 (40%) had no concerns. Using an FYI cutoff of ≥93%ile, 9/16 (56.2%) "ASD" sibs scored in this high-risk range, whereas, another 3 (18.8%) "ASD" sibs scored between 80 and 92%iles (moderate-risk range). Using the high-risk cutoff for ASD, sensitivity was 56.2% and specificity was 70.5% in this sample. Using the moderate-risk cutoff for ASD, sensitivity increased to 75% and specificity decreased to 37.7%. Further analyses of these data are in progress to determine the best cutoffs for 12-month screening.

Conclusions: The preliminary results from this longitudinal study support the utility of the FYI as an effective parent-report screening tool for 12-month old infants at-risk for ASD in a high-risk infant sibs sample. Future research will identify specific items/constructs that are most predictive of various developmental and diagnostic outcomes, as well as look at trajectories to age three when clinical diagnosis for ASD is more stable.

108.01 Prospectively Identifying Infants 'at Risk' of An ASD in An Australian Community-Based Sample: Results from the Social Attention and Communication Study (SACS). J. Barbaro* and C. Dissanayake, *La Trobe University*

Background: Children with an Autism Spectrum Disorder (ASD) typically do not receive a diagnosis until 3-years of age, despite many parents suspecting a problem before 12-months. Although early markers of ASDs have been found as early as 6-months, there is little research on the prospective identification of these children prior to 18-months of age.

Objectives: The objective in this longitudinal study was to determine whether routine monitoring of social attention and communication behaviours, within the Victorian Maternal and Child Health (MCH) service, can prospectively identify infants who will receive a diagnosis of an ASD, in an Australian community-based sample.

Methods: Two-hundred and forty one MCH nurses from 17 Local Government Areas in metropolitan

Melbourne were trained on developmental markers of ASDs in infancy. 22,168 children were then monitored at regular intervals on key items during four routine check-ups (8-, 12-, 18-, and 24-months of age) at their local MCH centre. All children deemed to be 'at risk' of an ASD at 12-months or older by showing a 'pattern' of failure on the key items were referred to the SACS for a thorough developmental and behavioural assessment. These children were followed up at 6-monthly intervals until 24-months of age, when the ADOS and ADI-R were administered.

Results: One hundred and twenty-three referrals were received. Of the 110 children assessed, 89 met criteria for an ASD (ascertainment rate for ASDs: 81%). With one exception, all remaining children met criteria for a developmental and/or language delay (DD/LD). Of the 10 12-month-olds who were referred to us, 90% showed signs of an ASD. Receptive language was the key ability within the cognitive profile that differentiated children with an ASD and DD/LD at 24-months of age. Data will also be presented on the behavioural items at each age that best predict a diagnosis of an ASD at 24-months.

Conclusions: The results indicate that it is possible to prospectively identify children with an ASD as early as 12-months of age via routine monitoring by community service providers in a community-based sample. Receptive language should be stringently monitored alongside social attention and communcation behavious in toddlers, as those children with very poor receptive language skills are more likely to traverse the trajectory towards an ASD.

108.02 Population Based Autism Screening Program Using MCHAT.

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Background: A previous study carried out by the Institute of Health CarlosIII of Spain proved a significant delay in obtaining an ASD diagnosis by Spanish families. The mean age at which the sample of 646families received an ASD diagnosis was 4.72years (SD 3.54years) -current children age was 14years-. Results showed that a part of this diagnosis delay was due to the inefficacy of primary health care services (basically paediatricians) to detect ASD and to make the specific referrals. This was the main reason to pilot an AutismScreeningProgram in the Spanish public HealthSystem that covers 100% of the general population using the *MCHAT/Spanish version* previously validated

Objectives:

To estimate the cost of the instauration and application of and AutismScreeningProgram in the general population.

To detect children with PDD before 30months and apply them a specialised intervention at a very early age that improves their prognosis.

To reduce the uncertainty and stress of the families that spend a mean of two years seeking for a definitive diagnosis since their first worries appeared.

To inform and improve awareness about ASD in Primary Care Services (through workshops for paediatricians and nurses).

Methods:

Population: 9883 children of a selected area of Madrid from (1st April2006 and 31st May2008) that attend to two compulsory paediatricians visits: vaccination at 18months (N=7024) and general follow-up at 24months (N=5728).

Procedure:

1. Handing over of the MCHAT questionnaire and the informed consent to the families with a possibility given to the medical professional (blind to the MCHAT result) to mark the questionnaire in the case of a personal suspect.

2. Telephone interview to the families of the positive cases following the flow-chart format for the exploration of each failed item (Robins, 2001).

3. Referral to the Childhood Psychiatry Unit for the specialised evaluation of the confirmed positives cases (ADOS-G, ADI-R, MERRIL PALMER –R, VINELAND, Mac Arthur and SCQ).

4. Referral to Early Intervention Programs of those cases finally diagnosed with ASD, SLI, developmental delays, etc.

5. Search of "false negatives" though a randomized sampling selection of negative cases in which a telephone interview exploring each DSM-IV-TR criteria for AutisticDisorder was carried out.

Results: Global response rate (total of children): **2909/9883**=29.43%
Total questionnaires received: 3341 (1880 from 18 months visit and 1461 from 24 months visit)
Response rate at 18months visit= **1880**/7024 (26.76%)
Response rate at 24months visit =**1461**/5728 (25.50)
Positive cases in the questionnaire that follows to the second step of the a telephone interview=537
Positive cases confirmed after the telephone interview =55
Evaluated cases=43
ASD cases=10 (the rest were SLI or global developmental delay) False negative found cases= 1 (Asperger Syndrome)

Prevalence: 3.8 per 1000

Conclusions: It is possible to reduce time needed to obtain a diagnosis of autism, to involve children earlier in intervention programs and to reduce family stress, however, it is not clear thus far if these population programs are effective in terms of their economical costs and if they are able to detect at that age less severe forms of ASD as Asperger Syndrome. Nevertheless we must to have into account the limits of our results due to the partial participation rate.

108.03 Screening Children Between 18 and 24 Months Using the Systematic Observation of Red Flags (SORF) for Autism Spectrum Disorders: a Follow-up Study. D. McCoy*, A. M. Wetherby and J. Woods, *Florida State University*

Background: The American Academy of Pediatrics recommends screening for autism spectrum disorders (ASD) in all children at 18 and 24 months of age. However, there is not yet a well-validated autism-specific screening tool for this age range. Initial research using the *Systematic Observation of Red Flags* (*SORF*) for ASD resulted in the identification of 9 *red flags* that distinguished children with ASD in the second year of life. Further research is needed to confirm and extend these findings in a larger sample of children.

Objectives: The major objectives of this prospective, longitudinal study of the FIRST WORDS® Project were: 1) to determine which red flags differentiate children with ASD from children with developmental delays (DD) and children with typical development (TD) between 18 and 24 months of age, and 2) to determine a total score and a number of red flags cut-off with high sensitivity and specificity for group membership.

Methods: Participants were selected from a general population sample of 6,581 children recruited with a broadband screener for communication delays. Videotapes of the *Communication and Symbolic Behavior Scales* (*CSBS*; Wetherby and Prizant, 2002) behavior sample were collected from 150 children 18–24 months of age who were later diagnosed with ASD (n = 60), DD in which ASD was ruled out (n = 30), and TD (n = 60); 54 of these children were included in the initial study. The archived video samples were reanalyzed using the *SORF*. The 29 behaviors included 0–2 ratings of the absence of typical behaviors and presence of atypical behaviors in the *DSM IV* domains.

Results: Of the 29 items on the *SORF*, a one-way ANOVA indicated 20 behaviors that significantly differentiated the ASD group from the DD and TD groups with medium to large effect sizes (Cohen's d), including the 13 red flags originally identified. The red flags included both a lack of typical and presence of atypical behaviors falling in all three domains of the *DSM IV*. An analysis of receiving-operator curves (ROC) using the 20 items resulted in a cut-off score predicting group membership with an area under the curve exceeding 94% and a sensitivity of 92% and a specificity of 81%. Based on a count of the number of the 20 red flags present, a cut-off of 8 resulted in a sensitivity of 87% and specificity of 84%. Large significant correlations were observed between the *SORF* total score for these items and the total score of both the *CSBS* (r = -.83) and the *ADOS* (r = .66).

Conclusions: The results indicate that 20 of 29 behaviors on the *SORF* can meaningfully differentiate children with ASD from children with DD and TD. The findings support previous research showing that early indicators for ASD are present and can be observed in the second year of

life. Further validation of the cut-off score is necessary to confirm the utility of the *SORF* as an interactive screening instrument with at-risk children at 18-24 months following a general population screening for social communication delays.

108.04 Toddler Autism Screening with M-CHAT and the CSBS-Infant Toddler Checklist. T. P. Gabrielsen*, M. Villalobos, B. Segura, N. Wahmhoff and J. Miller, *University of Utah*

Background: The American Academy of Pediatrics recommends all children be screened for autism spectrum disorders (ASDs) at 18- and 24-month well child visits unless a risk factor (parent, provider, or caregiver concern or a sibling with ASD) suggests earlier screening. Two relevant screening instruments include the Modified Checklist for Autism in Toddlers (M-CHAT; Robins et al., 2001) and Communication and Symbolic Behavior Scales Infant Toddler Checklist (CSBS-ITC; Wetherby & Prizant, 2002).
Objectives: We used both measures to examine the rates of positive and negative screens within one sample.
Methods: The EACH CHILD Study collaborated with a large community pediatric practice to implement systematic screening for ASD in toddlers. Over the six-month period of the study, 817 (81%) of eligible toddlers were screened. The screened group reflects the ethnic and socioeconomic diversity statewide. Both the M-CHAT and CSBS-ITC were administered. Authors' guidelines for cutoff scores were used to determine positive results for each measure (indicating concern for ASD). Researchers scored all questionnaires and contacted parents of children who screened positive. The M-CHAT phone interview protocol was followed for children with positive M-CHATs. Individual domains on the CSBS- ITC that were failed were re-administered by phone. If a child continued to screen positive after phone follow-up, an in-person screening with the Autism Diagnostic Observation Schedule (Lord et al., 2000) and Mullen Scales of Early Learning (Mullen, 1995) was offered. All forms were available in Spanish, and a Spanish speaker administered phone follow-up and in-person evaluations when appropriate.

Results: Results for the M-CHAT alone indicated that 14.6% children screened positive on the parent questionnaire, and 2.1% continued to screen positive after the phone follow-up (7.1% could not be contacted). In this group, of those who participated in the in-person evaluation, 7 (54%) showed significant early signs of autism by clinical judgment. Results for the CSBS-ITC indicated that 16.8% of children screened positive on the parent questionnaire, with 4.6% continuing to screen positive after the phone follow-up (5.9% could not be contacted). After in-person screening, 11 (48%) were believed to show significant early signs of autism. Two more children with significant signs of autism were not picked up by either the M-CHAT or CSBS-ITC, but were seen in person because of parent concerns, and found to have significant signs of autism by clinical judgment.
Conclusions: This is the first study to our knowledge to use both the M-CHAT and CSBS- ITC in the same sample. Children identified as showing early signs of autism were most likely to screen positive on both screeners, but 4 children screened positive on the CSBS-ITC alone. Phone follow-up reduced the number of false positives for both measures. The 2 cases identified as false negatives suggest that parent, caregiver, or provider concern is a valid reason for referral even if initial screeners show negative results.

108.05 The Early Screening for Autism and Communication Disorders (ESAC): Preliminary Field-Testing of An Autism-Specific Screening Tool for Children 12 to 36 Months of Age. A. M. Wetherby*[1], C. Lord[2], J. Woods[1], W. Guthrie[2], K. Pierce[3], S. Shumway[4], A. Thurm[4] and S. Ozonoff[5], (1)*Florida State University*, (2)*University of Michigan*, (3)*University of California, San Diego*, (4)*National Institute of Mental Health, National Institutes of Health*, (5)*M.I.N.D. Institute, University of California at Davis Medical Center*

Background: There is a critical need for validated screening tools for autism spectrum disorders (ASD) in very young children so that families can access intensive, appropriate intervention services as early as possible. The American Academy of Pediatrics (Johnson & Meyer, 2007) recommended that all children be screened for ASD at 18 and 24 months. However, there are no well-validated screening tools for this age range.

Objectives: The purpose of this study was to examine the utility of a new autism-specific parent report screening tool, the *Early Screening for Autism and Communication Disorders* (ESAC) to screen for ASD in children between 12 and 36 months of age.Methods: The research edition of the ESAC included 47 recognition format or closed-choice items based on research on early red flags of children with ASD from 12-36 months. It included items from all three DSM IV domains

on both the absence of typical milestones and the presence of atypical behaviors. Field-testing for the ESAC was conducted from two sources: 1) a follow-up of 375 children recruited by the FIRST WORDS® Project with a broadband screener for communication delays from a general population sample of 6,149 children; and 2) 75 children referred for possible ASD to 4 field-test sites in the US. The ESAC was evaluated for the 452 children in 3 age groups: Early 2nd year (12-17 months, *m*=15.2, *n*=136), Late 2nd year (18-24 months, *m*=20.5, *n*=145), and 3rd year (25-36 months, *m*=29.6, *n*=175). A best estimate diagnosis of ASD (*n*=136), developmental delay in which ASD was ruled out (DD; *n*=96), or typical development (TD; *n*=218) was made based on a diagnostic evaluation.

Results: Receiver operating curves (ROC) were examined for the entire 47 items and for a subset of 24 items that best discriminated children with ASD from the nonspectrum groups. The area under the curve for the 47-item and 24-item total scores ranged from .90 to .94 across the 3 age groups. Preliminary cutoffs were established for each age group with sensitivity ranging from .85 to .91, specificity from .82 to .84, PPV from .55 to .81, and NPV from .88 to .98. Moderate to large correlations (*r*= -.34 to -.54) were observed between the ESAC and nonverbal and verbal developmental quotients on the Mullen Scales of Early Learning. Large correlations (*r*=.57) were observed between the ESAC and the ADOS. False positives and false negatives were examined in relation to the DSM triad of diagnostic features.

Conclusions: These results provide preliminary support for the validity of the ESAC as an autism-specific screener in children 12-36 months age. These findings add to the research documenting the accuracy of parent report to screen young children. Using a parent report tool, such as the ESAC, minimizes the time required of healthcare providers, maximizes the role of the family, and provides reasonably accurate information about whether to refer a child for a diagnostic evaluation for ASD. These findings offer promise for a cost-effective screener for ASD in the 2nd and 3rd years of life.

Oral Presentations Program
109 Genetics

109.00 Under-Representation of African Americans in Autism Genetic Research: a Rationale for Inclusion of Subjects Representing Diverse Family Structures. C. Hilton*[1], K. M. Jackson[1], R. Fitzgerald[1], R. Maxim[2], C. Bosworth[3] and J. N. Constantino[1], (1)*Washington University School of Medicine*, (2)*Saint Louis University*, (3)*Special School District of St. Louis County*

Background: Differences in the contributors of genetic susceptibility to disease have been observed as a function of ethnic/ancestral origin for a number of medical and psychiatric conditions. African American children with autism are currently grossly under-represented in existing genetic registries and genetic studies of autism.

Objectives: In this retrospective analysis we explored barriers to participation of African American families in autism genetic research.

Methods: We estimated the number of autistic children of African American descent in our geographic region using CDC surveillance data from our Autism and Developmental Disorder Monitoring (ADDM) site. In this context, we reviewed the outcomes of our ongoing efforts to recruit and enroll African American families into either of two large national genetic registries: the Autism Genetic Resource Exchange (AGRE) and the Simons Simplex Collection (SSC). Over the period of this data collection, the requirements for both registries included availability of both parents and at least one full biological sibling.

Results: Extrapolating from the CDC 2002 St. Louis Autism and Developmental Disabilities Monitoring findings, we estimated that 730 African American children in metropolitan St. Louis, Missouri between ages 3 and 21 have an autism spectrum disorder. Of those, only 49% have received a clinical diagnosis by a medical service specializing in neurology, psychiatry, or developmental disorders (the usual sources of recruitment for autism genetic studies). We selected a clinical source serving the highest number of African American children with autism per year in our region, and identified 73 diagnosed children who were considered for enrollment in either SSC or AGRE. Of the 73 identified families, 28 had no siblings or no full siblings available to participate in the study, 17 could not be located from the contact information provided by the clinical service, 11 represented single-parent households with the other parent unable or unavailable to participate; 3 of the probands were adopted; 3 were born prematurely (and therefore excluded on the basis of registry criteria), 3 had comorbid developmental

conditions excluded by the retrospective registries. The remaining 12 (16%) qualified and enrolled.

Conclusions: Based upon these findings we estimate that without modifications to typical exclusion criteria, only 8% of all children of African American descent with ASD in our region would be identifiable through medical sources and eligible for inclusion in existing autism genetic registries. Comprehensive efforts--including the acceptance of participation of families of diverse structure--to facilitate the inclusion of African American children in existing registries is warranted. Any resulting compromise of the ability to establish identity by descent in genetic analyses may well be outweighed by availability of a critical number of African American probands to test and replicate genetic findings using case-control methods.

109.01 Limited Genetic Covariance Between Autistic Traits and Intelligence: Findings from a Longitudinal Community Based Twin Study. R. A. Hoekstra*[1], F. Happé[2], S. Baron-Cohen[1] and A. Ronald[3], (1)*University of Cambridge*, (2)*Institute of Psychiatry, KCL*, (3)*Birkbeck College, University of London*

Background:

Intellectual disability is common in individuals with autism spectrum conditions (ASC), but the prevalence of intellectual impairment may be overestimated in ASC due to ascertainment bias (Skuse, 2007). Therefore, the strength of this association is unclear and its relevance to finding the underlying (genetic) causes of ASC remains elusive. Furthermore, little is known about the longitudinal relationship between autistic traits and intellectual abilities. Instruments that assess autistic traits on a quantitative scale enable the study of this association in community based samples, free of the possible effects of ascertainment bias.

Objectives:

1) To investigate the association between autistic traits and intelligence in a large general population twin sample, both in the full-range scores and in the most extreme scoring 5% of this population. 2) To assess this association longitudinally over multiple time points in childhood. 3) To examine the etiology of this association.

Methods:

Parental ratings of autistic traits, using the Childhood Autism Spectrum Test (CAST, Scott et al., 2002), were collected in a sample of 8,848 twin pairs when the children were 8, 9, and 12 years old. Data on intelligence were collected when the twins were 7, 9, and 12 years. Phenotypic and longitudinal group correlations in the children with high CAST scores or with low IQ were compared to the associations among the full-range scores. The genetic and environmental influences on the overlap between autistic traits IQ and on the stability of this relationship over time were estimated using structural equation modeling.

Results:

Autistic traits were only modestly negatively related to intellectual ability, both in the extreme scoring groups and in the sample as a whole (r = -.14 to -.27). This association was mainly due to autistic trait items assessing communication difficulties. Cross-age correlations between CAST and IQ scores were similar to within-age correlations, and changes in autistic traits did not predict a change in intelligence, indicating that the modest association between these traits was stable over time. Genetic model fitting showed that autistic traits and IQ were influenced by a common set of genes and a common set of environmental influences that continuously affect these traits throughout childhood. The association between autistic traits and IQ was explained by genetic effects and by environmental influences shared between the twins. Importantly, the genetic correlation between autistic traits and IQ was modest (r_g = -.27)**.**

Conclusions:

The findings from this general population twin study suggest that whilst both autistic traits and IQ are stable traits across middle to late childhood, the association between these traits is consistently modest and driven by communication problems characteristic for autism. Individual differences in autistic traits are highly heritable and are substantially genetically *independent* of intellectual functioning. Future molecular genetic and neurobiological studies of ASC that seek to elucidate the pathways from genes to autism should include a focus on genetic influences that spare intellectual abilities.

109.02 Quantitative Autistic Trait Aggregation in Siblings of Autistic Probands in 1,246 IAN Families: Further Support for Differential Genetic Transmission of Simplex and Multiplex Autism. J. N. Constantino*[1], P. Law[2], A. Abbacchi[1], Y. Zhang[1], H. Lindsay[1] and C. Gruber[3], (1)*Washington University School of Medicine*, (2)*Kennedy Krieger Institute*, (3)*Western Psychologicial Services*

Background: Previous research has suggested that simplex and multiplex autism may involve divergent mechanisms of inheritance. In a previously published study involving 210 multiplex autism families and 80 simplex autism families, we observed differential patterns of familial aggregation of quantitative autistic traits (QAT) for males in simplex versus multiplex autism.

Objectives: To explore the aggregation of QAT in an independent sample of 1,101 self-identified simplex and 145 self-identified multiplex autism families, encompassing a total of 2,772 children in autism-affected families.

Methods: All data was acquired through the Interactive Autism Network (IAN), an internet-based volunteer register for U.S. families, for which eligibility includes: a) having at least one child diagnosed with an autism spectrum disorder (ASD) by a professional; and b) a full biological parent or legal guardian willing to participate. For this analysis we included families in which there existed: 1) a 4-18 year old ASD proband; 2) at least one full biological sibling in the same age range; and 3) QAT measurement for the proband and sibling(s) completed by parent-report using the Social Responsiveness Scale (SRS). 2,760 of these children were also rated by their parents using the Social Communication Questionnaire (SCQ).

Results: SRS and SCQ total scores were moderately correlated (ICC 0.62 for affected children), supporting substantial correspondence between quantitative severity and DSM-IV criterion endorsement. Principal components factor analysis of SRS data revealed a unitary factor structure, supporting use of singular (total) SRS scores in the data analyses. The QAT distribution for children in self-identified simplex autism families was distinctly bimodal, with a nadir in the distribution at an SRS T-score of 60, and a cluster representing unaffected siblings tightly grouped about a mean of 20.0. Of note is that 10 per cent of the children deemed unaffected by their families fell in the "pathological" cluster of the bimodal distribution. Although a bimodal distribution was also observed for females in multiplex families, the distribution for males in multiplex families was unimodal, i.e. without an appreciable cluster of unaffected children. The respective means for all boys whose SRS scores fell below a uniform quantitative severity threshold (60T) differed by 0.5 SD between simplex and multiplex families ($t=-3.85$; $df=633$; $p<0.001$). Affected children in both groups exhibited a wide, continuously-distributed range of severity.

Conclusions: We observed clear evidence of familial aggregation of continuously-distributed QAT in males in multiplex families, however most unaffected individuals in self-identified simplex families appeared to be devoid of aggregation of such traits—in essence they appeared categorically unaffected. A remarkable feature of the distribution of QAT in this large sample of simplex ASD families was the location of the notch in the bimodal distribution of parents' reported scores (the threshold at which 90% of families differentiated affected from unaffected children), which fell only 1.5 SD above the general population mean. These results support a hypothesis of differential genetic transmission of ASD in simplex versus multiplex families, and also indicate that traditional methods for designation of affected status may result in substantial underestimation of sibling recurrence risk.

109.03 Twin Concordance for Autism: a Comparison of Multiple Diagnostic Criteria in a Population-Based Twin Study. E. K. Schweigert*[1], M. A. Gernsbacher[1], R. L. Hefter[1], I. I. Gottesman[2] and H. H. Goldsmith[1], (1)*University of Wisconsin-Madison*, (2)*University of Minnesota*

Background: Despite assertions that autism is one of the most strongly genetically influenced multi-factorial developmental disabilities, evidence for the strength of genetic influences relies heavily on small English and Scandinavian twin studies ascertained with considerably more narrow diagnostic criteria than used today. Objectives: To examine contemporary evidence of the genetic contributions to autism and the autism spectrum using a twin study design.

Methods: The study design incorporated a two-pronged approach to participant ascertainment. First, we recruited families from Wisconsin birth records of twins born from 1998-2003, and we screened 3758 two to three year-old twins for

autism and the autism spectrum (Kees et al., 2005; Hefter et al., 2008). Second, we undertook statewide case-finding and recruited twins up to 20 years of age who had community diagnoses on the autism spectrum. Primary caregivers of children identified in both prongs were interviewed about each of their twins, using the Social Responsiveness Scale (SRS; Constantino et al., 2003) and the Social Communication Questionnaire (SCQ; Rutter, Bailey, & Lord, 2003), which contains content derived from the Autism Diagnostic Interview–Revised. We then visited the homes of families with at least one twin above cut-off scores on the SRS or SCQ, and we administered the appropriate module of the Autism Diagnostic Observation Schedule (ADOS). We examined extensive medical records, and (blind to zygosity and concordance) we excluded any twin pair in which another medical diagnosis could plausibly render an autism diagnosis nonidiopathic (seizures were not an exclusionary criterion). We analyzed twin concordance for having received a credible community diagnosis and scoring above the thresholds on the ADOS, SCQ, and SRS; uncertain zygosity was determined by genotyping.

Results: MZ pairwise concordance was at least twice DZ pairwise concordance for all measures: community diagnosis = MZ 65% (15/23), DZ 23% (7/31); ADOS-autism cut-off = MZ 53% (10/19), DZ 26% (5/19); ADOS-spectrum cut-off = MZ 77% (17/22), DZ 31% (9/29); SCQ = MZ 57% (12/21), DZ 19% (5/26); SRS-stricter cut-off = MZ 52% (12/23), DZ 11% (3/28); and SRS-broader cut-off = MZ 74% (17/23), DZ 26% (8/31). A combined criterion of ADOS-spectrum cut-off and SCQ led to a MZ pairwise concordance of 50% (10/20) and a DZ pairwise concordance of 15% (3/21), whereas a combined criterion of either ADOS-spectrum cut-off or SCQ led to a MZ pairwise concordance of 62% (13/21) and a DZ pairwise concordance of 17% (4/24). The male:female ratio was relatively consistent across the different diagnostic criteria: community diagnosis = 6.1:1; ADOS-autism cut-off = 5.6:1; ADOS-spectrum cut-off = 4.9:1; SCQ = 4.8:1; SRS-stricter cut-off = 5:1; and SRS-broader cut-off = 4.6:1. We also pursued model-fitting approaches to these data, which will be reported. Conclusions: These results confirm the classic twin studies in suggesting substantial genetic variance for the autism phenotype. However, unlike some of the classic results, MZ twin concordance is not near 100%, and DZ concordance does not approach zero. Implications for genetic models of autism are discussed.

109.04 Pursuit Eye Movement Abnormalities in First-Degree Relatives of Individuals with Autism. A. M. D'Cruz*, M. W. Mosconi, L. Ankeny, M. Kay, S. J. Guter, L. D. Stanford and J. A. Sweeney, *University of Illinois at Chicago*

Background: Pursuit eye movement precision is a heritable trait that enables visual tracking of moving targets. Two phases of smooth pursuit have been identified that engage separate, but overlapping, neural systems. The first 100ms of pursuit is referred to as the "open-loop" phase, and is driven by sensory analysis of target motion. Pursuit *after* the first 100ms of pursuit initiation is considered "closed-loop", and is more dependent upon predictions of target velocity and ongoing feedback about performance. Individuals with autism have demonstrated reduced open-loop accuracy for rightward-moving targets, as well as bilaterally reduced closed-loop pursuit accuracy. Pursuit performance in unaffected relatives of individuals with autism has not been systematically investigated, but may yield useful endophenotypes for the disorder.

Objectives: To investigate pursuit eye movements in first-degree relatives of individuals with autism.

Methods: Fifty-nine first-degree relatives (parents and siblings) of individuals with autism and 38 age- and IQ-matched healthy control individuals between 8-55 years of age performed a step-forward pursuit task. Participants initially maintained fixation of a central target, after which the target stepped 3 degrees left or right of center and then continued to move in the same direction at constant velocity. The latency and accuracy of the initial saccade made to acquire the target, as well as the latency and accuracy of the ensuing open- and closed-loop pursuit were measured.

Results: Relatives of affected individuals evidenced reduced open-loop accuracy to rightward targets and reduced closed-loop accuracy bilaterally, consistent with the pattern of results reported previously in individuals with autism. The latency and accuracy of the initial catch-up saccade and the latency of pursuit initiation did not differ between groups.

Conclusions: Family members of individuals with autism show deficits in pursuit eye movements

relative to controls that directly parallel findings we have previously described in an independent sample of autism probands. Reduced open-loop accuracy to rightward targets is a highly atypical finding, and suggests distinct disturbances in sensory processing of visual motion mediated by left extrastriate cortex, or in sensorimotor transformations by cortical eye fields and cerebellum. Additionally, bilateral reductions in closed-loop accuracy indicate impairment in the ability to use feedback about the accuracy of tracking to reduce error that is not hemisphere-specific. These findings are consistent with reports of altered functional connectivity in autism that may be more pronounced in the left hemisphere, as well as evidence of cerebellar pathology. Importantly, our findings suggest that such alterations and their impact may be familial, and thus provide a useful and highly specific neurophysiological endophenotype for autism research.

109.05 Phenomic Determinants of Genomic Variation in Autism Spectrum Disorders. Y. Qiao[1], N. Riendeau[1], M. Koochek[1], X. Liu[2], C. Harvard[1], J. Hildebrand[1], J. J. A. Holden[2], E. Rajcan-Separovic[1] and M. E. S. Lewis*[1], (1)*University of British Columbia*, (2)*Queen's University*

Background: Autism Spectrum Disorders (*ASDs*) are common, heritable neurobiologic conditions of unknown etiology confounded by significant clinical and genetic heterogeneity. Since ASDs are considered complex genetic disorders, resulting from the interaction of several genes and environmental factors, the lumping together of all cases of ASD, with no subgrouping based on phenotypic characteristics, makes the identification of contributory genes extremely difficult. The fact that autism is known to be associated with several distinct medical/genetic disorders further highlights its genetic heterogeneity. Thus, comprehensive "*whole body*" phenotyping and more accurate diagnostic methods are necessary to clarify the underlying co-morbidities, causes and symptoms of ASDs – inclusive of neurobehavioural, medical and morphologic traits. Array comparative genomic hybridization (array-CGH) technology has been used to rapidly screen the genome for pathogenic copy number variants (pCNVs) associated with ASD. Whilst current data suggests that pCNVs contribute to ASD pathogenesis, their role within a growing constellation of ASD microdeletion and microduplication syndromes remains poorly understood, due to the absence of consistent, standardized and comprehensive somatic, medical and neurobehavioural phenotyping of ASD subjects.

Objectives: To address this, we evaluated a broad categorization of phenotypic traits (or *phenomes*) for 100 subjects with ADI-R/ADOS-G confirmed idiopathic ASD undergoing 1Mb BAC array-CGH. We selected 100 subjects with "complex" ASD scores of ≥3 based on criteria modified from de Vries et al. (*J Med Genet* 2001) for array-CGH screening for CNVs, and summarize a systematic classification of clinical features present in those individuals with and without pCNVs.

Methods: We stratified our findings according to CNV type (pathogenic or benign) and total CNV load and reviewed detailed prenatal, medical, developmental and multi-generation family histories, assigning subjects to specific phenotypic subgroups based on co-morbidity with; (1) Intellectual Disability (ID; IQ<70); (2) presence of prenatal (intrauterine growth retardation) and/or post-natal growth anomalies; (3) micro-/macro-cephaly; (4) epilepsy; (5) craniofacial dysmorphisms; (6) congenital physical or systemic anomalies, (7) pregnancy complications; and, (8) neonatal complications.

Results: Array-CGH uncovered 9 different pCNVs found in 9/100 ASD subjects having complex phenotypes (ASD ± ID and/or physical anomalies) and normal routine karyotype, Fragile X, metabolic, targeted 22q11/22q13 and subtelomeric FISH findings. pCNVs included del(5)(p15.2-15.31) (2.4Mb), del(3)(p24.3) (0.1 Mb), dup(18)(p11.3)(0.9 Mb) and dup(7)(q11)(1.5 Mb). Recurrent pCNVs included del(2)(p15-16.1) (4.5 and 5.7 Mb) found in 2 unrelated subjects presenting with an ASD and ID. Deletion of 14q14.2 (0.7 Mb) and dup(15)(q11) (10 Mb) co-occurred in a niece-aunt relationship, resulting from abnormal segregation of a maternal cryptic balanced translocation. Maternally inherited del(X)(p11.22) (470 Kb) was uncovered in 2 autistic brothers with ID and cleft lip/palate. Male: female distribution of pathogenic CNVs was reduced to 1.25:1 from 3.2:1 in the original cohort. Phenotypic subgrouping confirmed greater CNV pathogenicity in subjects with microcephaly (p=0.04) and ID (p=0.02).

Conclusions: CNVs found in individuals with ASDs signal the locations of ASD-related culprit genes, and whole genome screening coupled with extensive phenotyping including medical and morphological assessments, is an efficient and

cost-effective approach to improve prediction of candidate genes and detect those of mild to moderate effect.

109.06 Association Study of a Linkage Region on Chromosome 3P25 in 816 Families Shows Strong Evidence for association of with Autism and Language Delay. J. Carayol[1], M. Letexier[1], F. Tores[1], R. Francis[1], R. Sacco[2], A. M. Persico[2] and J. Hager*[3], (1)*IntegraGen SA*, (2)*Univ. Campus Bio-Medico*, (3)*IntegraGen*

Background:

Autism is highly influenced by genetic factors. Genome-wide linkage and more recently association approaches have been used to identify autism genes. Two independent studies reported evidence for linkage to a region on chromosome 3p25 and a third association between a micro-satellite marker and autism in the same region. We performed a linkage scan in families from the AGRE collection and confirm linkage to this region on chromosome 3p25.

Objectives:

Identify the gene(s) underlying the replicated linkage signal on chromosome 3p25 using a high density, SNP genotyping and association study approach.

Methods:

228 SNPs were selected for genotyping. SNPs were selected with a MAF≥ 0.1 according to CEU-HAPMAP data. SNPs were genotyped using the SNPLex assay (Applied Biosystems). Initially we performed an association analysis in 493 autism families from the AGRE collection followed by a replication study of the positive markers in an independent sample of 323 families from Italy.

Results:

Six markers located in the ATP2B2 gene showed positive p-values. The strongest evidence for association was obtained for markers rs3774180 (p= 0.002) and rs2278556 (p= 0.004). All six positive markers were genotyped in the Italian replication set. All but one also showed positive association with the same allele, again rs3774180 and rs2278556 providing the strongest results (p= 0.002 and p= 0.006 respectively). The joint analysis of the 816 families resulted in strong evidence for association of the ATP2B2 gene with autism (rs3774180, p= $3.4x10^{-5}$, and rs 2278556, p= $1.4x10^{-4}$).

ATP2B2 codes for the brain specific calcium pump PMCA2. Calcium transport plays a major role in synaptic signal transmission and pathways associated with autism have been shown to depend on intra-cellular calcium concentrations. ATP2B2 is also expressed in the inner ear and has been shown to be involved in the modulation of hearing impairment. We therefore investigated if the association with autism could be more specifically linked with endophenotypes that may be dependent on hearing or the correct interpretation of sounds (e.g. language). We selected the ADIR-scores correlated with onset of language DEVT, AWORD and APHRASE. As this information was available only in the AGRE data only the 493 AGRE families were included in this sub-analysis. The family set was split into two for initial analysis and replication respectively (278 and 215 families). For DEVT a total of eight SNP markers showed significant p-values in the first family set, including all but one from the primary autism analysis. The strongest signal was obtained for markers rs6442169 (p= 0.003), which was moderately positive in the in the initial analysis and rs3774180 (p= 0.0039). Only one marker and two markers respectively showed positive association with APHRASE and AWORD. Marker rs6442169 replicated for DEVT in the 208 additional AGRE families. In the combined set the p-value was p= $1.9x10^{-4}$.

Conclusions:

We replicated a linkage signal on chromosome 3p25. SNP analyses in a total sample of 816 families provides strong evidence for association of the ATP2B2 gene with autism. More specifically, our results show that ATP2B2 may be involved in language delay in autism.

Oral Presentations Program
110 Neuroimaging

110.00 Early Brain Development in Toddlers with Fragile X Syndrome Compared to Toddlers with Autism. H. C. Hazlett*[1], A. A. Lightbody[2], M. D. Poe[1], A. Reiss[2] and J. Piven[3], (1)*University of NC*, (2)*Stanford University School of Medicine*, (3)*University of North Carolina*

Background: While the genetic basis of autism is not yet known, the genetics of fragile X syndrome (FXS) is well characterized. Both disorders share a number of behavioral characteristics, suggesting common neuropathology. Neuroanatomical

evidence suggests that brain enlargement may be a characteristic of both disorders.

Objectives: In this structural MRI study, we examined brain volumes in 52 young males (aged 18-42 months) with FXS (subdivided into those with and without autism), 63 males with autism, and 50 comparison cases (31 typically developing children and 19 children with developmental-delay).

Methods: We obtained total and regional gray and white matter tissue volumes for the subjects with FXS and compared them to the brain volumes of the children with autism and our comparison cases. Additionally, we measured the volumes of selected subcortical structures, such as the caudate nucleus and amygdala. As a secondary analysis, we also examined the brain volumes of boys with FXS who also met criteria for autism (FXS+Autism).

Results: Boys with FXS were observed to have enlarged total brain volume, and significantly enlarged cerebellar gray matter volume, compared to the controls. Volume of the basal ganglia structures, such as the caudate, globus pallidus and putamen, were enlarged in the boys with FXS compared to boys with autism or controls. No significant differences in hippocampal volume was observed. Children with FXS+Autism were observed to have a different profile of brain volume enlargement compared to children with autism. Specifically, children with FXS+Autism had significantly enlarged caudate volumes, but significantly smaller amygdala volumes.

Conclusions: The ability to distinguish the neurobiological phenotypes of FXS and autism may provide important clues to the pathogenesis of autism. Clearly the study of biological mechanisms underlying autistic behavior in etiologically-defined subgroups such as those with fragile X syndrome, is an important and probably under-employed strategy for dealing with the heterogeneity of autism.

110.01 Relationship Between Surface Area, Brain Volume, and Cortical Thickness in Young Males with Autism. R. K. Lenroot*[1], D. M. Nielson[1], D. O. Black[2], S. J. Spence[1], A. Thurm[2], S. E. Swedo[2], F. M. Lalonde[2] and J. N. Giedd[2], (1)*NIH*, (2)*National Institute of Mental Health, National Institutes of Health*

Background: Increasing evidence indicates that brain growth in children with autism may be accelerated early in life and then slow, resulting in more significantly enlarged brain volumes in younger children (Courchesne, Neuron 2007). Development of surface area and thickness of the cortex may be affected by different factors (Rakic, Science 1988), but the relationship of these aspects of cortical structure has not been previously described either in young children or in children with autism.

Objectives: Characterize cortical morphometry including surface area and cortical thickness in a cohort of young males with autism.

Methods: Subjects: 44 males meeting strict criteria for Autistic Disorder (age 4.8(s.d. 1.1)) and 31 healthy male age-matched controls (age 4.3(s.d. 1.3)). Diagnoses were established by trained raters using the ADOS and ADI-R. IQ was assessed on a subset of subjects using a hierarchy of tests, including the WASI, Mullen, WPPSI, DAS-II, or WISC-R. The mean IQ of the autistic subjects was 56.8 (s.e. 1.78, n=36); and for healthy controls the mean was 117.9 (s.e. 3.58, n=26). Autistic subjects were sedated during MRI procedure; controls were not sedated. All subjects were scanned using the same 1.5T scanner and protocol (Giedd, Cerebral Cortex 1996). Measures of surface area, average cortical thickness, and gray and white matter volumes for total cerebrum and lobar regions were obtained using the fully automated CIVET pipeline developed by the Montreal Neurological Institute (Ad-Dab'bagh, Neuroimage, 2006). Group comparisons were performed in SPSS using one-way ANOVA with age as a covariate. Relationships between cortical features were analyzed using stepwise linear regression and partial correlation.

Results: Total brain volume (926.0 (s.e. 15.8) vs 1033.5 (s.e. 13.2), $F=26.3$, $p<.001$), gray matter in all regions and occipital white matter volumes were increased in autistic subjects. Surface area and mean cortical thickness were increased in all regions in subjects with autism. Both surface area and cortical thickness significantly predicted variation in gray matter volume, with the greater contribution from surface area. Regression analysis of the relation between surface area and cortical thickness including age, diagnosis, cortical thickness, and interaction of age and cortical

thickness found all terms to be significant, suggesting a different relationship between area and cortical thickness in autistic subjects than healthy controls. Subsequent partial correlation analysis controlling for age found a significant correlation between area and cortical thickness in typical controls (pr=.509, p =0.005) but not autistic subjects (pr=.145, p=.346). A similar pattern of results was also found across brain regions except for the occipital lobe, in which neither group showed significant correlation.

Conclusions: Increased brain volumes in young males with autism are associated with both increased surface area and increased cortical thickness. We did not find the same correlation between surface area and cortical thickness in autistic subjects as in healthy controls, which may relate to early abnormal neurodevelopment.

110.02 Cerebral Organization in Young Children with Autism. C. W. Nordahl*[1], T. J. Simon[2], K. Camilleri[2], S. J. Rogers[1], S. Ozonoff[3] and D. G. Amaral[2], (1)*M.I.N.D. Institute, University of California at Davis*, (2)*University of California, Davis*, (3)*M.I.N.D. Institute, University of California at Davis Medical Center*

Background: Abnormalities in cerebral organization have been reported in individuals with autism, but few studies have focused on very young children. Brain volume appears to follow an altered developmental trajectory in individuals with autism, yet the timing and nature of early overgrowth has not been adequately examined. Aberrant sulcal organization and connectivity patterns have also been reported in older individuals with autism, but extension of these findings to younger children has not been fully explored.

Objectives: To evaluate multiple aspects of cerebral organization in a large sample of 2-4 year old children with autism spectrum disorders. Analyses include total cerebral volume and cortical sulcal organization, a putative measure of connectivity. This study was carried out in the context of the M.I.N.D. Institute's Autism Phenome Project.

Methods: Structural MRIs were acquired in 107 children (49 autism [AU], 24 autism spectrum disorders [ASD], 34 typical development [TD]), ages 27-56 months (mean 40 months). Diagnostic instruments included the Autism Diagnostic Observation Schedule – Generic (ADOS-G) and the Autism Diagnostic Interview – Revised (ADI-R). Children with typical development did not have any siblings with autism or any known developmental, neurological, or behavioral problems. Additional exclusionary criteria were limited to those with physical contraindications to MRI. Volumetric analyses included measurements of the total cerebrum. Surface-based morphometry was used to generate sulcal depth maps to evaluate cortical folding patterns.

Results: In males, age was correlated with total cerebral volume in the TD group (r = .49, p = .01) but not in the AU (r = -.02; p = .9) or ASD (r = = .4, p = .1) groups. In males 27-42 months of age, total cerebral volume was significantly enlarged in the AU group relative to the TD group (p = .03). The ASD group did not differ significantly from either the AU or the TD group. Preliminary analyses of sulcal depth maps suggest that children with AU and ASD have abnormalities in sulcal organization in superior temporal regions as well as the intraparietal sulcus; areas typically associated with biological motion and attentional control respectively.

Conclusions: Preliminary data show that boys with autism spectrum disorders do not have typical age related growth in total cerebral volume. Brain enlargement is present in children with autism under the age of 3.5 years. Regional abnormalities in sulcal organization are also present in young children with autism, suggesting an abnormal pattern of connectivity in functionally relevant brain regions early in development.

110.03 Changes in the Developmental Trajectories of Striatum in Autism. M. Langen*, H. G. Schnack, H. Nederveen, D. Bos, B. E. Lahuis, M. V. de Jonge, H. van Engeland and S. Durston, *Rudolf Magnus Institute of Neuroscience, University Medical Center Utrecht*

Background: Autism is a severe neurodevelopmental disorder that is characterized by impaired social interactions, impaired language development and repetitive, rigid behavior. Studies of brain changes in autism have often focused on the first two clusters of symptoms, despite the prominence of repetitive behavior in this disorder: in many cases these symptoms onset early in development and often form a significant impairment for affected individuals. Many studies have associated the basal ganglia with repetitive and stereotyped behavior across a range of neuropsychiatric disorders. In autism, conflicting reports of changes in the basal ganglia

have been published. However, the *developmental trajectory* of the basal ganglia has not been examined in this disorder and conflicting results may in part reflect differences in developmental stage between samples. In this study, we investigate brain development cross-sectionally in high-functioning autism.
Objectives: To examine brain development in a homogeneous sample of subjects with high-functioning autism.
Methods: Structural MRI scans were acquired from 188 individuals aged between 6 and 25 years (99 subjects with high-functioning autism and 89 typically developing, matched controls). Twelve subjects with autism were using neuroleptic medication. An automatic image processing pipeline was used to determine the volume of total brain, gray and white matter of the cerebrum, cerebellum and lateral ventricle volumes. Basal ganglia structures were traced manually. Regional changes in the basal ganglia were investigated using voxel-based morphometry with correction for multiple comparisons using false discovery rate (alpha < 0.05, two-tailed). Multivariate analysis of variance was used to investigate differences in brain development between diagnostic groups, with diagnosis as a fixed factor and age as a co-variate. Linear and quadratic curves were fitted to investigate the shape of the developmental curves. To investigate the relationship of basal ganglia volume with behavior, correlations with measures of repetitive and stereotyped behavior were calculated.
Results: Developmental trajectories of the caudate nucleus, putamen and nucleus accumbens differed between subjects with autism and controls. Results were not accounted for by overall changes in brain volume or neuroleptic medication. The development of the caudate nucleus differed from typical most, as its volume increased with age in autism, while it decreased for controls. Voxel-based analysis showed that changes in striatum localized to the head of the caudate nucleus. Overall caudate nucleus volume was associated with repetitive behavior in autism.
Conclusions: We report changes in striatal development in autism, where caudate volume is associated with repetitive behaviors. This emphasizes the importance of striatum in the etiology of autism, in particular in the development of repetitive behavior that characterizes the disorder.

110.04 Auditory Processing Differences in Autism Spectrum Individuals with and without Language Delay: An fMRI Study.
F. Samson*[1], T. A. Zeffiro[2], A. Mendrek[3], K. L. Hyde[4] and L. Mottron[1], (1)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (2)*Neural Systems Group, Massachussetts General Hospital*, (3)*Centre de Recherche Fernand-Seguin, Université de Montréal*, (4)*Montreal Neurological Institute, McGill University*

Background: Autism spectrum (AS) individuals exhibit widely differing language developmental trajectories. While some individuals show a delay in language acquisition, echolalia, stereotyped language and pronoun reversal, others do not. Delays in language acquisition might be associated with atypical development of the connections among the cortical regions involved in auditory and language processing.

Objectives: The present objective was to test if developmental language acquisition differences in AS individuals may be related to differences in auditory cortical processing of sounds of varying spectral and temporal complexity.

Methods: Using a 3T MRI system, we studied 27 AS and 13 typically developing (TYP) individuals while they listened to eight auditory stimuli constructed by crossing two carrier signals (pure and harmonic tones) with four levels of modulation depth (0, 25, 50 and 100%). Participants were asked to detect the presence or absence of the modulations. In order to investigate the association between the timing of language acquisition and auditory system development, language delay (first words after 24 months/first sentences after 33 months) was used as a grouping variable. The three groups were matched on IQ (FSIQ, VIQ and PIQ), age (mean: 22yr 9mo), sex and manual preference. The Language Delay (LD) and Non Language Delay (NLD) groups were also matched on their ADI scores (Social, Communication and Repetitive behaviours). Activation patterns within auditory and language specific brain regions, including the transverse temporal gyrus (TTG), superior temporal gyrus (STG) and inferior frontal gyrus (IFG) were examined for the TYP, NLD and LD groups.

Results: There were no between-group task performance differences in response time and accuracy. For both the pure and harmonic carrier signal tones, the linear LD>NLD>TYP contrast revealed more primary auditory cortex and IFG (BA 45/47) activity. The TYP>NLD>LD contrast

showed greater activity in non-primary auditory areas (STG and middle temporal gyrus, BA22) and in the IFG (BA 44). There were no between-group differences in spectral complexity processing as examined in the harmonic vs. non-harmonic condition contrast. Non-primary auditory areas were more sensitive to temporal complexity increases (modulation depth) in the TYP group while the reverse contrast (LD>NLD>TYP) revealed no significant activity.

Conclusions: These results indicate that auditory processing of complex stimuli more strongly engages primary auditory areas in the LD group relative to the NLD and TYP groups while non-primary auditory areas and areas outside the auditory cortex are engaged less strongly. The level of task-related activity in the NLD group was intermediate between the LD and TYP groups. This suggests that the differential atypical low-level auditory processing in the LD and NLD groups may follow the clinical distinction made between autism and Asperger syndrome. At this stage however, it is not possible to determine if the observed differences in auditory processing are a cause or an effect of variable language delay.

110.05 Default Mode Network in Patients with High Functioning Autism Spectrum Disorders during Resting State fMRI. L. Miller[1], K. Jagannathan[1], J. O'Boyle[2], R. T. Schultz[3], M. Stevens[4], R. Sahl[1], G. Pearlson[4] and M. Assaf*[4], (1)*Institute of Living, Hartford Hospital*, (2)*Trinity College Dublin*, (3)*Children's Hospital of Philadelphia and the University of Pennsylvania*, (4)*Institute of Living, Hartford Hospital / Yale University*

Background: Autism Spectrum Disorders (ASD) are characterized by deficits in social and communication processes. It has been suggested that brain-wide reduced functional connectivity, including in the default mode network (DMN), might underlie these deficits. Past research has found that activation of the DMN, a brain network that is activated during passive task states, is related to social and emotional processing and that its connectivity might be impaired in ASD.

Objectives: 1) To compare DMN strength of functional connectivity of ASD patients to matched Healthy Controls (HC) during fMRI resting state scan using Independent Component Analysis (ICA); and **2)** to evaluate the correlation between DMN strength of functional connectivity and severity of patients' symptoms as measured by the Autism Diagnostic Observation Schedule (ADOS).

Methods: Resting state fMRI data with no cognitive task were collected from fifteen high functioning ASD patients and fifteen HC matched on age, gender and race. was used to identify the DMN. Group differences were examined using random effect two sample t-tests and multiple regression analysis was used to measure the correlation between DMN connectivity strength and ADOS scores. All analyses were corrected for age and IQ.

Results: The results indicated that within the DMN, patients showed significantly weaker strength of regional activity in the posterior cingulate gyrus and the precuneus. Correlation analysis showed that as patients had more severe symptoms as measured by the ADOS, they had less regional connectivity of the precuneus, a key region in DMN.

Conclusions: Our data suggests that ASD patients show decreased connectivity in the default mode compared to HC and that this abnormal connection correlates with their symptom severity. Due to the simplicity and the short time span of resting state scans, this method can be applied to lower functioning and younger individuals and possibly used as a biomarker for Autism in future genetic and treatment studies. This work was supported by Autism Speaks and Hartford Hospital .

110.06 Amygdala Enlargement in Toddlers with Autism Related to Severity of Social and Communication Impairments. C. M. Schumann*, C. Carter Barnes and E. Courchesne, *University of California, San Diego*

Background: Autism is a heterogeneous neurodevelopmental disorder of unknown etiology marked by social, emotional and communication impairments. The amygdala has long been a site of intense interest in the search for neuropathology in individuals with autism, given its well established role in the production and recognition of emotions and modulatory role in social behavior. Previous studies suggest that the amygdala undergoes an abnormal growth trajectory in individuals with autism that includes a period of early overgrowth, followed by diminished growth at older ages, which parallels an abnormal cortical growth trajectory albeit extends to a later age. However, this pattern is

not well characterized, particularly at young ages when the symptoms of autism first become apparent.

Objectives: To 1) measure amygdala volume in toddlers with autism compared to age- and gender-matched, typically developing children and 2) evaluate potential relationships between amygdala size and the severity of behavioral impairments.

Methods: Eighty nine toddlers (n= 66 males, 23 females) participated between the ages of 18-60 months as part of an ongoing longitudinal MRI study. We measured amygdala volume on each toddler's MRI scan taken closest to 3 years of age using previously published tracing methods (Schumann et al., 2004). Each child then returned at ~5 years of age for a final clinical evaluation, which included the ADOS, ADI-R, and IQ exam.

Results: Toddlers at 3 years of age who later received a confirmed diagnosis of autism (32 males, 9 females) compared to typically developing toddlers (28 males, 11 females) had a larger right ($p<.01$) and left ($p<.05$) amygdala volume, when gender and age at MRI were considered covariates. When each gender was analyzed separately, and covaried for age at MRI scan, autistic males had a significantly larger right amygdala volume ($p<.05$) and autistic females had a significantly larger left ($p<.01$) and right ($p<.01$) amygdala volume compared to age- and gender-matched typical toddlers. Correlation analyses revealed a significant relationship of amygdala volume with the severity of social and communication impairments on the ADI-R and in toddlers with an autism spectrum disorder. In males, but not females, with autism, right ($r=.51$, $p<.01$) and left ($r=.55$, $p<.01$) amygdala volume was correlated with the ADI-R Social scores. Also in males, but not females, with autism, there was a significant negative correlation of Vineland Communication score and right ($r=.41$, $p<.05$) and left ($r=.37$, $p<.05$) amygdala volume.Conclusions: This study provides further evidence that the amygdala undergoes an abnormal growth trajectory in children with autism, and that the overgrowth begins at least by three years of age, often before the diagnosis is typically given. In toddlers who eventually receive a diagnosis of autism, the degree of amygdala enlargement at three years of age is associated with the severity of their social and communication impairments at five years of age. However, males and females differed in their neuropathological and behavioral profiles, where females more robustly differed from typical in amygdala volume and males showed a significant relationship of amygdala size with the severity of their social and communication impairments.

Lifetime Achievement Award and Presentations Program

111 From Infancy to Imaging: Autism and the Developmental Psychology of Marian Sigman

Speakers: P. C. Mundy[1] C. Kasari[2] S. Bookheimer[2] (1)*UC Davis*, (2)*University of California, Los Angeles*

This talk will review the major contributions Dr. Marian Sigman has made to the field of autism research over the past 30 years. Dr. Peter Mundy will talk about Dr. Sigman's interest in infant attention and the joint attention research they carried out together at UCLA. He will discuss how the translation of theory and measurement of the development of infant social attention to the study of autism with Marian, Connie Kasari & others had an impact on developmental psychopathology. Dr. Connie Kasari will present research findings on Dr. Sigman's interest in emotional development and relationships, and how these research findings influenced her newer work on interventions for children with autism and their families. Dr. Susan Bookheimer will discuss the CPEA and ACE imaging centers that Dr. Sigman's lead at UCLA, the expansion of her collaborations into autism genetics and functional imaging of social communication, and the future directions of the autism center she created.

111.00 Student and Developing Country Travel Awards.

111.01 Introductory Remarks.

111.02 From Infancy to Imaging: Autism and the Developmental Psychology of Marian Sigman. P. C. Mundy[1], C. Kasari[2] and S. Bookheimer*[2], (1)*UC Davis*, (2)*University of California, Los Angeles*

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of autism with Marian, Connie Kasari & others had an impact on developmental psychopathology. Dr. Connie Kasari will present research findings on Dr. Sigman's interest in emotional development and relationships, and how these research findings influenced her newer work on interventions for children with autism and their families. Dr. Susan Bookheimer will discuss the CPEA and ACE imaging centers that Dr. Sigman's lead at UCLA, the expansion of her collaborations into autism genetics and functional imaging of social communication, and the future directions of the autism center she created.

112 Poster II

112.01 1 Analysis of Increased Functional Diversity by Alternative Splicing in Autism Candidate Genes. C. Hicks*, J. Del Greco, A. Tchourbanov and G. Steinhardt, *Loyola University Medical Center*

Background: Alternative pre-mRNA splicing generates multiple protein isoforms from a single gene, thereby contributing to functional and proteome diversity. Alternative splicing regulates gene expression. Its biological role in biomedical research can be dramatically amplified when the protein isoforms generated serve as potential biomarkers or therapeutic targets. While many studies have focused on alternative splicing prediction, its impact on protein function in candidate genes associated with common diseases, in particular neuropsychiatric disorders, such as autism have received little attention.

Objectives: Analyze the impact of alternative splicing on protein function in autism.

Methods: We performed computational analysis of alternative splicing in 238 autism candidate genes. We hypothesized that alternative splicing affects protein function and increases functional diversity.

Results: We have shown that more than 80% of autism candidate genes are alternatively spliced, and demonstrate that alternative splicing events involve structural deletions, insertions, and substitutions. The number of protein isoforms generated per candidate gene ranged from 1 to 17. About 40 genes had complete deletion of functional domains.

Conclusions: Knowledge discovery and comparative genomic analysis showed increased functional diversity, which could potentially contribute to phenotypic plasticity and diversity.

112.02 2 Familial Relationship for Anti-Human Brain Antibodies in Autism Spectrum Disorders (ASD). P. E. Goines*[1], D. Braunschweig[2], R. Boyce[2], P. Ashwood[3] and J. Van de Water[2], (1)*University of California, Davis*, (2)*University of California at Davis*, (3)*M.I.N.D. Institute, University of California at Davis*

Background: Autism spectrum disorders (ASD) may result from a gestational insult that alters neurodevelopment. Mothers of children with autism have a higher incidence of circulating antibodies directed towards fetal brain proteins than mothers of typically developing (TD) children. Some children with autism also produce brain-targeted autoantibodies in contrast to age-matched TD controls. It is currently unknown whether mothers with antibodies toward fetal brain proteins are maternally related to ASD subjects producing brain-directed antibodies.

Objectives: Explore a familial relationship in autoantibody production through comparison of human brain autoantibodies in plasma from autism and control subjects whose mothers have been pre-screened for fetal brain-reactive IgG.

Methods: Subjects are children of mothers previously tested for plasma anti-fetal brain IgG. Plasma from ASD and TD control children was analyzed using western blot for reactivity to human hypothalamus, cerebellum, fetal, and whole adult brain protein medleys. Reactivity to brain proteins was compared with respect to familial relationships, as well as the developmental outcome of the child.

Results: Preliminary results suggest that children of mothers with antibodies to fetal brain proteins have equal chances of developing IgG to brain proteins as children of non-reactive mothers. Thus, it appears as though there is little to no correlation between the presence of autoantibodies in the mothers of children with autism and autoantibodies to brain proteins in their offspring.

Conclusions: A mother-child relationship regarding anti-brain IgG may indicate a strongly heritable predisposition towards autoimmunity. Alternatively, maternal IgG-related interference in fetal neurodevelopment may cause production of brain reactive-IgG in the child. A lack of correlation suggests that anti-brain IgG in mothers and children may represent distinct etiologies/ manifestations of ASD.

112.03 3 Using Perceptual Signatures to Link Genotype with Neural Alterations in Autism Spectrum Disorder (ASD) and Fragile X Syndrome (FXS). J. Hanck[1], K. Cornish[1], A. Chaudhuri[1], C. Kogan[2] and A. Bertone*[3], (1)*McGill University*, (2)*University of Ottawa*, (3)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*

Background: The functional link between genetic alteration and behavioral end-state manifested in different neurodevelopmental conditions is rarely straightforward. As suggested by Belmonte & Bourgeron (2006), in order to study convergent and/or divergent neuro-cognitive phenotypes between genetically dissociable conditions, analysis at a neural network level must be considered. Objectives: To introduce a theoretical framework and paradigm that characterizes neural endophenotypes (Muller, 2007) underlying visual information processing in ASD and FXS, defined by characteristic information processing abilities referred to as perceptual signatures (reflect the integrity of neural networks mediating visual information processing; Bertone & Faubert, 2006). We argue that perceptual signatures may be useful for differentiating ASD and FXS from each other at a neural network level, and for providing a better understanding of plausible causal mechanisms underlying atypical information processing in each condition. Methods: Based in part on results from a series of studies assessing static and dynamic information processing in high-functioning autism and fragile x syndrome (FXS), perceptual signatures of the two conditions were compared. Given that similar perceptual paradigms were used to assess functioning for both conditions, a direct comparative with limited methodological constraints was possible. Results: The resulting perceptual signatures are consistent with a pattern of perceptual performance that is condition-specific only for luminance-defined information conditions. In general, enhanced sensitivity to luminance-defined static information is evidenced for the ASD group only whereas decreased sensitivity to simple dynamic information defines FXS performance. Decreased sensitivity to texture-defined information is manifested in both groups. These results suggest that neural networks mediating low-level information processing in ASD and FXS are divergent, or condition-specific, at the local neural network level only; the perceptual consequence of altered integrative neural networks mediating complex, texture-defined information are convergent, or non-specific (Bertone et al., 2003,2005; Kogan et al., 2004). Conclusions: We present a data-driven, causal model associating genetic perturbation with neuromodulatory consequences on local network connectivity that is specific to ASD and FXS. The model suggests altered lateral connectivity within primary visual areas in ASD, and dorsal-stream related dysfunction in FXS as the most biologically plausible type of atypical connectivity congruent with their respective perceptual signatures. We argue that this intermediate level of analysis is useful for suggesting condition-specific neural etiology, and for guiding genetic research by restricting the search for candidate genetic origins most consistent with the neuromodulatory effects on low-level networks underlying perceptual abilities in ASD and FXS. This suggestion is especially important within the context of evidence suggesting that atypical information processing may be one of autism's core deficits (Belmonte et al., 2004). Finally, such a theoretical framework is shared by others who support genetically-influenced, systemic neural models where causal genetic perturbations alter neural connectivity (and also tissue morphology), leading to atypical information processing capabilities which may at least in part define neurocognitive phenotypes manifested in ASD (Herbert, 2005) and FXS.

112.04 4 Autism Traits and Schizotypal Traits in a Genetic Syndrome (47,XXY): The Role of Executive Functioning. S. Van Rijn*[1], A. Aleman[2], L. de Sonneville[1] and H. Swaab[1], (1)*Leiden University*, (2)*University of Groningen*

Background: Klinefelter syndrome is an X chromosomal condition (47,XXY karyotype) that is present in about 1 in 700 boys. Because of the risk for development of psychopathology, it has been suggested that studying individuals with the 47,XXY karyotype may help in the search for cognitive, neural and genetic mechanisms underlying psychopathology.
Objectives: The aim of this study was to assess levels of autism traits and schizotypal traits in individuals with XXY. We explored the relationships between specific domains of autism traits and specific domains of schizotypal traits. Secondly, our study was focused on executive functioning in this population in order to gain insight in putative underlying mechanisms that may help explain increased risk for symptoms in both the autism and schizophrenia spectrum. Methods: 44 XXY men and 46 non-clinical controls were included in the study. Autistic traits were measured using the Autism Spectrum Questionnaire. The Schizotypal Personality

Questionnaire was used for measuring levels of negative, positive and disorganized schizotypal traits. Both are a dimensional self-report measures. We assessed mental flexibility using the Shifting Set Task of the Amsterdam Neuropsychological Tasks (ANT) program. Results: Levels of autism traits and schizotypal traits were substantially higher in the XXY group. The effect size (Cohen's d) were 1.9 for the autism sumscore and 1.23 for the schizotypy sumscore. Scores on all individual subscales of the AQ and SPQ were significantly higher in the XXY group, with effect sizes ranging from 0.6 to 1.73. The total AQ score was significantly correlated with the total SPQ score, more specifically with negative and disorganized schizotypal dimensions. This was mostly due to high correlations between these SPQ dimensions and the subscale 'dividing attention' of the AQ. In the Shifting Set Task, which requires mental flexibility and attentional control, the XXY group made more errors (effect size 0.5) and had longer reaction times (effect size 0.9).
Conclusions: These findings call for a clinical investigation of vulnerability to autism and schizophrenia spectrum pathology in Klinefelter syndrome. Our findings stress the importance of studying the role of executive dysfunctions, particularly in the area of attentional control, as a vulnerability factor for developing both autism features as well as schizophrenia-like symptoms. Genetic syndromes associated with increased vulnerability for both autism- as well as schizotypal features, such as Klinefelter syndrome, may help in gaining insight in common underlying mechanisms.

112.05 5 Birth Order Effects on the Phenotypic Expression of Autism in Multiplex Families. L. A. Martin*, T. Pike, K. Shier, B. Vaudrey, B. Benson and M. Shelby, *Azusa Pacific University*

Background:

Autism Spectrum Disorders or ASDs include autism, Asperger syndrome, and pervasive developmental disorder not otherwise specified (PDD-NOS). ASDs are characterized by disturbances in social behavior, impaired communication and the presence of stereotyped behaviors or circumscribed interests. Most cases of ASD remain idiopathic. A few recent studies indicate that some cases may be caused by immunological abnormalities while other studies point to a strong genetic component. Whatever the cause, recent estimates indicate that ASDs are on the rise with the current prevalence reported by the CDC of 1 in every 150 births (Keuhn, 2007). Interestingly, previous studies have found birth order effects on the phenotypic expression of autism in families with more than one affected child (multiplex families; Lord, 1992; Spiker, 2001; Reichenberg, 2007). The rise in ASDs, as well as the presence of birth order effects, suggests that some cases are influenced by environmental factors.

Objectives:

Through this study, we further explore the effects of birth order on phenotypic expression of ASD in multiplex families. The examination of birth order effects on autism symptom severity may provide important clues to the etiology of ASD. For example, the demonstration of increased ASD severity in each subsequently affected birth may point towards a dosage-type effect of either genetic or environmental factors.

Methods:

We utilized pre-existing data from the Autism Genetic Resource Exchange (AGRE) consisting of test scores from children with ASD from multiplex families. ASD was determined by the Autism Diagnostic Interview-Revised (ADI-R) and/or Autism Diagnostic Observation Schedule (ADOS). Mean test scores from the Vineland Adaptive Behavior Scales (VABS), Peabody Picture Vocabulary Test (PPVT) and Ravens Colored Progressive Matrices (RCPM) were compared between first-born and later-born children with ASD. ASD children from multiplex families were also divided into first-born, second-born, and third-born groups for additional analyses. Over 1600 individuals with ASD from nearly 800 multiplex families were included in the study although data from each test was not available for each individual. It was hypothesized that the phenotypic expression of ASD would increase with each subsequently affected child within a family. Therefore, later-born children should be more severely affected and thus perform worse on cognitive tests than first-born children from multiplex families.

Results:

Results showed that there was a significant decline RCPM scores between first-born and later-born children. ANOVA revealed a significant

progressive decline in these scores from first-born to third-born children with ASD. Results from the PPVT also demonstrated a significant decline in scores from first-born to later-born children. However, while the means progressively decreased from first-born to third-born children with ASD, the decrease was only significant between first-born and second-born and first-born and third-born children. Results of the VABS comparisons are also reported.

Conclusions:

The results support our hypothesis of an increase in the phenotypic expression of ASD with each subsequently affected child in multiplex families. The significant decline in test scores of cognitive ability supports the idea of a dosage-type effect *in utero* in some multiplex families. The dosage effect may be due to either environmental or genetic factors.

112.06 6 D-Cycloserine Enhances Social Cognition in An Animal Model Relevant to Autism. M. E. Modi* and L. J. Young, *Emory University*

Background: Social bonding in the highly affiliative, socially monogamous prairie vole is a complex cognitive process involving social motivation, integration of social information, and social learning and memory. We propose that an assay of social bonding may be an effective approach to identify novel pharmacotherapies for the treatment of the social deficits associated with neuropsychiatric disorders, such as autism. In the laboratory, social bonding is assessed by measuring partner preference. Previous studies in prairie voles have implicated an interaction between the oxytocin (OT), dopamine (DA) and glutamate (Glu) receptor systems in nucleus accumbens (NA) in the formation of partner preferences. In this study we directly examine the role of the Glu receptor system in social bonding using two clinically-relevant compounds that target ionotropic Glu receptors, D-cycloserine (DCS) and Ampakine CX614. The Glu receptor system functions in the cellular encoding of learning and memory and has been utilized in the clinical setting to enhance cognitive processes. We hypothesize that by enhancing Glu neurotransmission with these compounds, partner preference formation will be accelerated.
Objectives: To determine the effect of glutamate receptor enhancers on social cognition as measured through partner preference formation in prairie voles and to assess the usefulness of this model in identifying novel pharmacotherapies for the treatment of social deficits.
Methods: In Experiment 1, DCS and Ampakine CX614 were injected intraperitoneally (IP) in female prairie voles. DCS was tested at doses of 0, 10, or 20 mg/kg and CX614 was tested at doses of 0, 1, 5 and 10 mg/kg. After injection the females were paired with a male for six hours. This cohabitation typically does not produce partner preferences in our colony. Following cohabitation, the females were tested for partner preference formation. Time spent in social proximity to either the partner or stranger was quantified in the partner preference apparatus
In Experiment 2, DCS was site-specifically infused into socially relevant or control brain regions of female prairie voles. The animals were cannulated and injected with 10 µg per side of DCS directly into the NA, medial amygdala (MeA) and caudate-putamen. The animals were then paired with males for 6 hrs, and tested for partner preference

Results: Animals receiving 0, and 20 mg/kg doses of DCS IP failed to form a partner preference for their partner. In contrast, females that received 10 mg/kg IP did form a partner preference. CX614 did not promote partner preference formation. Microinjection of DCS into the NA and the MeA induced partner preference formation whereas a control injection did not.
Conclusions: DCS accelerated partner preference formation in female prairie voles, suggesting that this drug enhances social cognition. We hypothesize that by enhancing glutamatergic transmission in the nucleus accumbens, we are expediating the process of social learning, potentially through interactions with the oxytocin system. Future studies will test the hypothesis that combined oxytocin and DCS will act synergistically to accelerate social bond formation in female prairie voles. If this hypothesis is correct, we predict that a similar combined therapy may be useful in ameliorating the social cognitive deficits in autism.

112.07 7 Comorbidities in Adult Attendees of a Specialist Autism Clinic. D. Spain*[1], T. J. Lavender[2], C. Wilson[3], S. Reed[4], E. Daly[5], M. Craig[5], D. Robertson[4], Q. Deeley[5] and D. Murphy[1], (1)*King's College London, Institute of Psychiatry*, (2)*Institute of Psychiatry*, (3)*University of Aberdeen*, (4)*South London & Maudsley NHS Trust*, (5)*Institute of Psychiatry, King's College London*

Background: Prior research has reported individuals with Autistic Spectrum Disorders commonly suffer from co-morbid mental health problems, for example, social anxiety disorder, Attention Deficit Hyperactivity Disorder, and Oppositional Defiant Disorder (Simonoff et al, 2008). However so far research has been limited to those diagnosed as children, or individuals with learning disabilities (mental retardation). Moreover, nobody has investigated the mental health characteristics of (non autistic) adults who present to services seeking a diagnosis of autism.

Objectives: To investigate the mental health of adults who present (for the first time) seeking a diagnosis of autism. .

Methods: We examined 298 consecutive referrals (mean age 33 years) to a specialist out-patient clinic for adults with ASD the Maudsley Hospital, London. The assessment consisted of an in-depth psychiatric interview and additionally the Autism Diagnostic Interview (ADI) or the Autism Diagnostic Observation Shedule (ADOS).

Results: Of the 298 referrals, 110 (38%) were given a diagnosis of ASD. In those who were positively diagnosed as having an ASD, 61% had a single comorbid disorder, and 24% had two or more comorbid disorders. The commonest comorbidities were depressive disorder (18%), Obsessive Compulsive Disorder (OCD) (15%), ADHD (12%) Generalised anxiety disorder (GAD) (7%), Social Phobia (6%) and schizophrenia (6%).

In patients where a diagnosis of ASD was not made, 80% received an alternative diagnosis. Of these the commonest were depressive disorder (30%), personality disorder (19%) GAD (14%), OCD (13%), ADHD (12%) and schizophrenia (8%).

Conclusions: The burden of additional mental disorder in adults with ASD is very high. In our service most adults who seek a diagnosis of autism do not have the disorder; but the vast majority of these 'negative ASD' cases do have other significant mental health problems. Of those who are diagnosed with ASD the majority have previously unrecognised co-morbid mental health problems requiring treatment.

112.08 8 Rates of Psychiatric Comorbidity in Children with High Functioning Autism and Asperger's Syndrome. R. Mahajan* and S. H. Mostofsky, *Kennedy Krieger Institute, Johns Hopkins University School of Medicine*

Background:

In addition to the diagnostic features of qualitative impairments in reciprocal socialization, communication and restricted/repetitive behavior, children with autism are vulnerable to comorbid conditions, especially other psychiatric disorders. These may further complicate the developmental trajectory and affect their functional outcomes. In spite of some recent efforts to characterize these comorbid disorders, there is a paucity of empirical investigations into the prevalence of the comorbid psychopathology and the nature of the relationship of the DSM-IV psychiatric disorders to the core features of Autism Spectrum Disorders (ASD).

Objectives:

To examine the rate of psychiatric comorbidity in children with high functioning autism (HFA) or Asperger's syndrome (ASP).

Methods:

The presence of comorbid psychiatric diagnoses was examined in a cohort of 71 children (10 girls and 61 boys) with HFA (n=35) or ASP (n=36) , aged 8 through 12 years (mean age 9.9 years +/- 1.58 years; mean FSIQ 99 +/- 15.87). These subjects were recruited as part of an ongoing neuroimaging and behavioral study; children with a history of epilepsy or known genetic diagnosis were excluded from participation. Diagnosis was confirmed with ADI-R and ADOS-G. A computerized parent interview, the Diagnostic Interview for Children and Adolescents-IV –Parent version (DICA-IV) was used to examine for the presence of psychiatric comorbidity.

Results:

Attention Deficit Hyperactivity Disorder (ADHD), Oppositional Defiant Disorder (ODD), Phobias (Simple and Social), Obsessive Compulsive Disorder (OCD), Generalized Anxiety Disorder (GAD), and Mood disorders were present in both ASP and HFA. Chi-square analyses revealed no significant between-group (HFA vs. ASP) differences in the rate of comorbidity for any of these diagnoses: Criteria for ADHD were met in 20% of those with ASP and 13% of those with HFA. Criteria for ODD were met in 20% of

subjects with ASP and 10% in those with HFA. Criteria for Simple or Social Phobias were met in 28% of those with ASP and 23% of those with HFA. Criteria for OCD were met in 6% of those with ASP and 11% of those with HFA. Criteria for a past diagnosis of Major Depressive Disorder (MDD) was met in 8% of ASP and 3% of HFA had and one subject with HFA met criteria for a Dysthymic Disorder. None of the subjects in either group met criteria for Bipolar Disorder, Separation Anxiety Disorder, Panic Disorder, Somatization Disorder, or for a current diagnosis of MDD.

Conclusions:

Children on the autism spectrum, whether HFA or ASP, experience significant comorbid psychopathology. These findings highlight the importance of carefully examining these disorders, as they are potential targets for effective treatment.

112.09 9 A Comparison of Parent and Teacher ADHD Ratings in Children with Autism. D. A. Pearson*[1], K. A. Loveland[1], M. G. Aman[2], C. W. Santos[1], R. Mansour[1], S. M. Elliott[1] and L. A. Cleveland[1], (1)*University of Texas Medical School at Houston*, (2)*Ohio State University*

Background:

Parents and teachers of children in the general school-age population have been noted to perceive behavioral adjustment in the same children quite differently. Specifically, teachers are often more sensitive raters of disruptive behaviors and classroom-related behaviors, while parents are more sensitive raters of internalizing difficulties. To date, little is known about the concordance of parental and teacher ratings of emotional adjustment in children with autism. Many children with autism have been noted to have significant symptoms of ADHD, which is associated with a number of co-morbid internalizing and externalizing problems.
Objectives:

The purpose of this study was to compare parent and teacher ratings of core ADHD symptoms (e.g., inattention, hyperactivity, impulsivity), as well as behavioral and emotional problems commonly comorbid with ADHD (e.g., oppositional behavior, anxiety).

Methods:

Participants were 60 children (46 boys; mean age=9.3 yrs; mean IQ=81) who met DSM-IV criteria for autism on the ADI-R and the ADOS. Parent and teacher behavioral ratings were compared on the Conners Parent Rating Scale (CPRS-R) and Conners Teacher Rating Scale (CTRS-R), using correlational methods.

Results:

Significant positive correlations between parent and teacher ratings suggest that parents and teachers perceive both some symptoms similarly in the same child: cognitive problems/inattention (p<.001), hyperactivity (p<.001), oppositional problems (p<.001), and social problems (p<.05)—but not anxiety (p=.31) or perfectionism (p=.85).

Conclusions:

Findings suggest that parents and teachers perceive core symptoms of ADHD and commonly co-morbid externalizing problems (e.g., oppositional behavior) in a similar manner, that their perceptions of internalizing problems (e.g., anxiety) are less similar. It is hypothesized that although the child may display similar patterns of ADHD symptoms in the home and school environments, that they may present differently in these two environments with regard to more internalizing behaviors such as anxiety.

112.10 10 Comorbidity of Bipolar Disorders in Children and Adolescents with Diagnosis of Autism Spectrum Disorders. N. M. Mukaddes*[1], S. Herguner[1] and C. Tanidir[2], (1)*Istanbul University, Istanbul Faculty of Medicine*, (2)*Istanbul University*

Background: The reported rates of Bipolar disorders(BP) in individuals with diagnosis of autism spectrum disorders (ASD) have shown great discrepancies, varying between 2.8% to 27% .The difference between the results of these studies seems related with methodological difficulties.
Objectives: The present study aimed to assess the rate of bipolar disorders in high functioning children and adolescents with diagnosis of Autism spectrum disorders.
Methods: Participants were from a private psychiatry center located in central city in Istanbul and autism clinic of child psychiatry department ,Istanbul School of Medicine. Ninety –Five individuals , 65 with diagnosis of Asperger's disorder(AS) and 30 with diagnosis of autistic disorder(AD) ,age ranged between 6-20 years

old(mean age:11.07+/_3.5) were included. Diagnosis of Asperger's Disorder and Autistic disorder were made based on DSM-IV criteria. Only subjects with full IQ over 70 in WISC-R were included in the study. Co-morbidity of BP was assessed using the Schedule for Affective Disorders and Schizophrenia for School Age Children - Present and Lifetime Version (K-SADS - PL). Final diagnosis of BP was made based on Leibenluft's " the narrow phenotype" definition. Therefore, only subjects who meet the full criteria in DSM-IV-TR for hypomania or mania, including the duration criterion and also hallmark symptoms of elevated mood or grandiosity were diagnosed with BPD.
Results: 4 out of the 95 subjects received the diagnosis of Bipolar Disorders(4.2%).All were male.3 out of the 65 subjects with AS (4.4%)and 1 out of the 30 subjects with AD (3.3%)got the additional diagnosis of BP.
Conclusions: It could be concluded that BP is not a rare co-morbid condition in youth with diagnosis of ASD . Differential diagnosis of BPD disorder in subjects with ASD seems crucial in establishing an effective treatment program, and therefore improving mental health outcomes.

112.11 11 Psychiatric Disorders in Optimal Outcome Children with a History of Autism Spectrum Disorders. K. Tyson*, E. Troyb, M. Rosenthal, M. Helt, I. M. Eigsti, L. Naigles, M. Barton and D. Fein, *University of Connecticut*

Background:

Children with Autism Spectrum Disorders (ASDs) exhibit symptoms that, historically, have been considered part of a lifelong disorder. ASDs are defined by marked deficits in social interaction, communication, and repetitive or stereotyped patterns of behavior. A small, but 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. Fein, Dixon, Paul, & Levin (2005) suggest that one outcome of children with ASD may be a resolution of symptoms into ADHD. Although researchers have found evidence for an array of co-occurring psychiatric disorders in children with ASD, few studies have explored the psychiatric histories of children who lose their ASD diagnosis.

Objectives:

The current study examines the prevalence of psychiatric disorders (other than ASD) in this small subset of children who were diagnosed with ASD before age 5, but who no longer meet criteria for an ASD diagnosis and are placed in mainstream classrooms. This study refers to children in this group as optimal outcome (OO) children.

Methods:

We compared prevalence rates for psychiatric disorders in 20 typically developing children (mean age = 13.23), 11 children with high-functioning autism (HFA) (mean age = 13.09), and 17 OO children (mean age = 12.91). Groups did not differ in gender ($p = .33$), age ($p = .50$), or WASI full-scale IQ ($p = .68$). We administered The Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version (K-SADS-PL) to children's parents in order to compare lifetime rates of different disorders across the three different groups.

Results:

Overall, one or more psychiatric disorders were present in 3/17 of control children (total 4 past, 0 present diagnoses), in 9/11 of HFA children (14 past, 12 current), and in 14/17 of OO children (15 past, 9 current). Notably, two out of 20 (10%) of control children, 3/11 of HFA children (27%), and 10/17 (59%) of OO children met diagnostic criteria for a past or present specific phobia (e.g., animal type, loud noises). No control children, 5/11 (45%) of HFA children, and 4/17 (24%) of OO children met diagnostic criteria for a past or present tic disorder or Tourette's disorder. One control child out of 20 (5%), 3/11 (27%) of HFA children, and 1/17 (6%) of OO children met criteria for past or present Major Depressive Disorder. No control children, 3/11 (27%) of the HFA children, and 7/17 (41%) of the OO children met criteria for past or present ADHD. Although the DSM-IV does not allow a diagnosis of ADHD along with ASD, evidence of ADHD symptoms in these children is of interest because of treatment implications.

Conclusions:

These preliminary results suggest that these Optimal Outcome children display a history of

psychiatric disorders more than their typically developing peers. OO children may show vulnerability to additional psychiatric conditions to a similar extent compared to HFA children. However, further research including a larger HFA sample is needed to support this conclusion.

112.12 12 Problem Behavior, Social Functioning and Academic Achievement in School-Aged Children with An Autism Spectrum Disorder. V. Rivera*[1], A. M. Estes[1], J. Munson[1], L. M. Elder[1], K. Burner[1] and P. Cali[2], (1)*University of Washington*, (2)*University of Illinois at Chicago*

Background:

It is well established that social impairments are directly related to autism spectrum disorders (ASD). However, there has been limited research regarding academic achievement in children with ASD. Studies have shown a relationship between social competence, problem behavior, and academic achievement in typically developing children and children with developmental delays without autism (DD), yet it remains unclear how these may relate in children with ASD.

Objectives:

This study aims to (1) compare academic achievement in 9-year-olds with ASD and DD, (2) investigate whether social functioning and problem behaviors at age 6 predict academic achievement in children with ASD at age 9, (3) examine whether social functioning and problem behaviors at age 9 are associated with academic achievement at age 9.

Methods:

Participants were children diagnosed with ASD (n=32) or DD (n=17) with an IQ greater than or equal to 70. Data for this study was collected during a larger longitudinal study that investigated early predictors of outcomes in ASD. Social functioning and problem behaviors were measured using the Battelle Developmental Inventory (teacher and parent report) and the Social Skills Rating System (teacher report) at age 6 and 9. Academic achievement and IQ were measured using the Differential Ability Scale at age 9.

Results:

Children in the ASD group demonstrated higher academic achievement scores in spelling, word reading and basic number skills compared with same-age children in the DD group. Within the ASD group, when controlling for IQ, fewer problem behaviors at age 6 were predictive of better spelling and word reading abilities at age 9. Basic number skills at age 9 were not associated with social or behavioral functioning at age 6. Within the ASD group, when controlling for IQ, no relationship was found between social and behavioral functioning at age 9 and academic achievement at age 9. Further analyses will extend this investigation of the relationship between academic achievement and social and behavioral functioning.

Conclusions:

Preliminary results suggest that children with ASD demonstrate higher academic achievement when compared with same-aged children with DD, even when controlling for IQ. There was a significant relationship between behavior problems at age 6 and academic achievement in spelling and word reading at age 9. This suggests that behavior regulation may set the stage for increased academic success in children with ASD. Future research exploring the relationship between academic achievement, behavior regulation and social competence may provide a basis for new educational and intervention strategies.

112.13 13 Correlation of Measures of Autistic and Obsessive-Compulsive Symptoms. R. Mullaney*[1], P. Johnston[2], C. Ecker[2], A. Jassi[1], A. Russell[3], E. Daly[4], D. Murphy[2] and M. R. C. AIMS Consortium[1], (1)*Institute of Psychiatry*, (2)*King's College London, Institute of Psychiatry*, (3)*Department of Psychology*, (4)*Institute of Psychiatry, King's College London*

Background: Obsessive-Compulsive symptoms are common in Autism Spectrum Disorders (ASD) (Russell et al. (2005); McDougle et al. (1995); Zandt et al (2006). It has been suggested that the high comorbidity of ASD and OCD may be explained by the repetitive behaviours typically present in ASD. However nobody has directly tested this hypothesis

Objectives: To correlate severity of Obsessive or compulsive symptoms and Autistic symptoms.

Methods: 40 Right-handed male subjects age 16-45 with ASD were diagnosed using both the ADI and ADOS, and we included a similar number of age matched controls. This investigation formed part of the MRC UK AIMS Network at the Institute of Psychiatry. Obsessionality was

measured using the Obsessive-Compulsive Index - revised version (OCI-R).

Results: 54% of people with ASD scored above the cut off for OCD, as compared to 10% of controls. Autism Quotient scores (AQ) were positively correlated with OCI-R scores overall. However there was no correlation between repetitive or compulsive behaviours (as measured using sub scores of the ADI and ADOS) and the OCI-R scores.

Conclusions: The prevalence of Obsessive-compulsive symptoms is much higher in subjects with an ASD than in the general population; but this is not explained by severity of autistic repetitive behaviours. It is likely therefore that they have a separable genetic and/or biological basis.

112.14 14 Patterns of Psychotropic Medication Use in Children with Autism Spectrum Disorders. L. M. Elder*[1], J. Munson[1], A. M. Estes[1], B. King[2] and G. Dawson[3], (1)*University of Washington*, (2)*University of Washington and Children's Hospital and Regional Medical Center*, (3)*Autism Speaks, UNC Chapel Hill*

Background: Increasingly, children with Autism Spectrum Disorders (ASD) are being treated with psychotropic medications, many of which have not been studied in children. Research on medication use in this population is typically conducted through survey methods using cross-sectional data. A longitudinal approach provides the advantage of capturing sequences in medication trials as well as other patterns of medication use.

Objectives: This study prospectively examines medication use in children with ASD, aged 2 – 10 years. This study has four objectives; to assess the proportion of children using psychotropic medications, to describe patterns of polypharmacy, to investigate usage by medication class, to examine age of initiation, and to describe the average length of medication trials by class.

Methods: This sample of 75 children with ASD participated in a multidisciplinary, longitudinal study on behavioral and neurobiological predictors of outcome in autism. Participants received diagnostic assessments at 3-4, 6 and 9 years of age. Every six months from age 3 through 11, parents participated in a telephone assessment of their child's medication use. Parents were asked to list medications their children took each month.

Results: Preliminary results indicate 52% of children used at least one psychotropic medication between age 2 and age 10. At age two, 0% of children were using a psychotropic medication, 8% used medication at age three, 13% at age four, 24% at age five, 31% at age six, 36% at age seven, 40% at age eight, 31% at age nine, and 34% at age ten. Of the children receiving psychotropic medication, 28% received two or more medications for at least three months, and 10% received three or more medications. The proportion of children on each medication class and average age of initiation by class include: stimulant (17%; 7.4 years), antidepressant (17%; 6.6 years), antipsychotic (9%; 6.7 years), other psychotropic (7%; 7.1 years), anticonvulsant (5%; 8.1 years), antiparkinsonian (1%; 6.3 years), and anxiolytic (0.7%; 6.5 years). Average length of trial was 11 months for stimulants, 18 months for antidepressants, 12 months for antipsychotics, 19 months for other psychotropics, 15 months for anticonvulsants, 25 months for antiparkinsonians, and 12 for anxiolytics. Further analyses will also explore the sequence of medication use, specific medication use within each drug class, and child characteristics associated with medication use.

Conclusions: Psychotropic medications are frequently used in children with ASD. Over half of children with ASD in this sample were prescribed a psychotropic medication at some point between the ages of 3 and 10. The percentage of children on psychotropic medication increased from age 2-6 and appeared relatively stable from 7-10 years. Stimulants were the most common class of psychotropic medication used, followed by antidepressants and antipsychotics. The current study provides information about the use and timing of medications in children with ASD. Findings suggest individual medications and medication combinations that should be studied further, and may inform future clinical trials.

112.15 15 Psychiatric Symptom Profiles of a Sample of Children with Asperger Syndrome. J. Bebko*[1], J. H. Schroeder[2] and J. A. Weiss[3], (1)*York University*, (2)*York University, Toronto*, (3)*Centre for Addiction and Mental Health & York University*

Background: There is increasing identification of psychiatric co-morbidities in individuals with Asperger syndrome that extend beyond the central diagnostic features of the disorder. Previous research indicates that depression, anxiety, obsessive-compulsive behaviours, and

attentional issues are more common in the AS population than they are in the general population.

Objectives: This study aims to examine the behavioural profile of non-referred individuals with Asperger syndrome (AS), and to determine the relations among psychiatric symptom scales.

Methods: Fifteen children with AS (6-18 years) participated in this study. Inclusion criteria included: no history of developmental language delay and average or above average cognitive and language functioning. The Childhood Behavior Checklist (CBCL), a parent-report measure with strong empirical support, was used to assess behavioural, emotional, and social problems. The Peabody Picture Vocabulary Test-III yielded an estimate of receptive language ability, and the Expressive One-Word Picture Vocabulary Test-2000 was administered to provide an estimate of expressive language ability. The Wechsler Abbreviated Scales of Intelligence was used to determine cognitive ability. Parents completed the Krug Asperger's Disorder Index to help to determine if the child's profile was characteristic of Asperger syndrome or autism. The Childhood Autism Rating Scale and the Autism Diagnostic Interview-Revised provided an estimate of the severity of autism symptoms.

Results: One-sample t-tests revealed significant differences between the AS group and typically developing norms (Mean t-score = 50) for all symptom scales and DSM-IV scales. Eighty percent of participants had at least one symptom score in the clinical range. The scales that were most commonly in the clinical range in this sample were Thought Problems, Anxiety Problems, Social Problems, OCD, and Attention Problems. Correlational analyses will be conducted to determine the relations between each of the scales.

Conclusions: This paper suggests that individuals with AS are at significant risk for associated psychiatric symptoms, and it is important to further investigate these linkages. It also highlights the importance of considering how these symptoms impact each other. Finally, it emphasizes the importance of determining the efficacy of current or modified treatments on these disorders in individuals with AS.

Funding: CIHR-NAAR Autism Spectrum Disorders Strategic Training Program (JJAH-PI), SSHRC, CIHR

112.16 16 Multi-Informant Ratings of Psychiatric Symptom Severity in Children with Autism Spectrum Disorders: The Importance of Environmental Context. S. M. Kanne*[1], A. Abbacchi[2] and J. N. Constantino[2], (1)*University of Missouri*, (2)*Washington University School of Medicine*

Background: Individuals diagnosed with an ASD often have concomitant emotional and behavioral difficulties that have a significant impact on their functioning. Knowing prevalence rates of psychiatric symptoms in individuals with ASD and understanding of how these psychiatric symptoms are reported across settings directly impacts diagnostic decisions and treatment planning. Interpretive challenges exist when this information is discrepant or contradictory. Despite the weight clinicians give to reports of psychiatric symptoms from various settings (e.g., parents and teachers), few researchers have examined the nature of cross-informant reporting differences in individuals with ASD.

Objectives: The objectives of this study were threefold: a) we examined a consecutively ascertained population of children and adolescents diagnosed with ASD to estimate the prevalence rates of comorbid psychiatric syndromes and sought to determine whether the various symptoms were either present, absent, or manifested in a range of severity in this clinical sample; b) we examined the extent to which parents and teachers agreed on quantitative characterization of these symptom domains in youth with ASD and their siblings; c) we attempted to elucidate domains of symptoms that might be better appreciated in home/family environments versus educational settings.

Methods: This sample included youths with autism spectrum disorders (n=177) and their siblings (n = 148), all phenotypically characterized using the Child Behavioral Checklist (CBCL), C-Teacher Report Form (C-TRF), Social Responsiveness Scale (SRS)-parent report; SRS teacher-report was also available in 98% of the cases. All ASD diagnoses were given by a professional clinician and were confirmed using the ADI-R and/or the ADOS.

Results: In ASD, parents reported substantial comorbidity with affective (26%), anxiety (25%), attentional (25%), conduct (16%), oppositional

(15%), and somatic problems (6%). Teachers reported a much lower prevalence: affective (6%), anxiety (15%), attentional (12%), conduct (2%), oppositional (9%), and somatic problems (3%). Autistic severity scores for children with ASD exhibited moderate correlations with general psychopathology within- but not across-informants, whereas sibling correlations were significant both within- and across-informants.

Conclusions: This study indicates a large proportion of individuals with ASD also display significant emotional and behavioral difficulties. In contrast to non-ASD siblings, when an ASD-affected child manifests more severe ASD symptoms in a particular setting, they also manifest more psychiatric symptoms. Informants across settings were discrepant in their ratings of psychiatric symptoms, especially internalizing symptoms, and more so in children with ASD compared to siblings. These discrepancies likely represent variations in state characteristics manifested in different contexts. This pattern of results supports the role of environmental context differentially affecting individuals with ASD. Implications for this study support the role of environmental context in psychiatric symptom expression in children affected by autism and suggest that informant discrepancies may more provide critical cues for these children via specific environmental modifications.

112.17 17 Reliability and Validity of the Children's Interview for Psychiatric Syndromes-Parent Version (P-ChIPS) in Youngsters with Autism Spectrum Disorders. A. N. Witwer* and L. Lecavalier, *Ohio State University*

Background: Research has shown that youngsters with ASDs present with high rates of behavior and emotional problems, including tantrums, mood swings, aggression, self-injury, and irritability. Psychiatric disorders are also quite prevalent; the most commonly-reported are disruptive behavior, mood, and anxiety disorders. Researchers have begun to examine psychiatric disorder in ASD using structured interviews. However, little research has examined the reliability and validity of these instruments, which are considered the gold standard in psychiatric research. One such interview is the *Children's Interview for Psychiatric Syndromes-Parent Version (*P-ChIPS)*.* It is a structured interview designed to concisely assess psychopathology according to DSM-IV criteria in clinical and epidemiological research with children and adolescents 6 to 18 years old.

Objectives: This study examined the reliability and validity of the P-ChIPS in children and adolescents with ASDs. We investigated the agreement between the P-ChIPS and the Child and Adolescent Symptom Inventory (CASI; a parent-completed DSM-IV-based measure of psychiatric disorders) on the assessment of mood, anxiety and disruptive behavior disorders. We will also measure internal consistency and assess interrater reliability.

Methods: The parents of 60 children and adolescents (mean=11.2±3.8 years; range 6-17) with autism, Asperger's disorder, and PDD-NOS were interviewed with the P-ChIPS and completed the CASI rating scale. The youngsters were administered the Stanford-Binet Intelligence Scales-Fifth Edition, and all had IQs>40. Diagnosis of ASD was confirmed by the Autism Diagnostic Interview-Revised. Agreement between the P-ChIPS and CASI was assessed with kappa statistics and overall agreement. The impact of IQ (IQ>70 vs. IQ<70), age (6-11 vs. 12-17 years), and language (verbal vs. nonverbal) on agreement was also examined by calculating kappa coefficients separately and comparing with z tests.

Results: Diagnostic agreement between P-ChIPS and CSI was higher for the disruptive behavior disorders and for major depression/dysthymia. Kappa statistics range from .20-.56 for the disruptive disorders, indicating fair to moderate agreement. Overall agreement ranged from 65-90%. Kappa statistics for the mood disorders were .35 and .22, indicating fair agreement. Overall agreement was 83% and 78%. Agreement was lower for the anxiety disorders, with most kappa coefficients indicating poor agreement (range .12-.48) and overall agreement ranging from 62%-80%. Age and IQ did not significantly influence kappa statistics.

Conclusions: Kappa statistics and overall agreement was lower than values reported in non-ASD samples. Age and IQ did not appear to impact kappa values. The P-ChIPS shows promise in the population, but may require adaptations for the ASD population.

112.18 18 The Complexity in Assessing the Overlap Between ADHD and ASD – a Review of Clinical Methods and the Neurobiological Evidence. N. Skokauskas*[1], L. Gallagher[1], A. Mulligan[2], J. Sander[1] and K. Johnson[3], (1)*Trinity College*

Dublin, (2)*University College Dublin*, (3)*Trinity College Institute of Neuroscience*

Background: Attention Deficit Hyperactivity Disorder (ADHD) and autistic spectrum disorders (ASD) are early onset neurodevelopmental disorders of childhood. Both are sexually dimorphic with males affected four times more frequently than females. Although DSM-IV-TR recognizes that over activity and inattention are frequent in ASD, but a diagnosis of ADHD is not made if ASD is present. This view has been challenged and there has been considerable debate of late concerning co-morbidity between ASD and ADHD. This topic is of scientific and clinical interest because it raises important questions about possible underlying mechanisms between ASD and ADHD. A better understanding of overlap between ADHD and ASD could indicate directions for further studies to find shared genetic vulnerabilities.

Objectives: to identify, review and analyse research findings, conclusions and methodologies on the overlap between ASD and ADHD. This paper also aims to discuss the limitations to the approaches utilised to date and to make suggestions for future research.

Methods: electronic databases and hand searches were made of the literature concerning clinical overlap, methods of assessing it and the underlying neuropsychological deficits.

Results: 23 relevant studies were identified, reviewed and included in this paper. Majority of the studies reviewed paid little or no attention to possible artifacts in the detection of co-morbidity between ASD and ADHD (for example referral and screening/surveillance biases, overlapping diagnostic criteria). This could explain remaining uncertainty about the extent and the nature of co-morbidity and disparate findings reported. Moreover majority of studies failed to address a key question: whether co-morbidity between ADHD and ASD actually exists, is artifactual or simply represents overlap of symptoms between the two conditions. On another hand what one might be conceiving as overlap between ADHD and ASD might actually be a reflection of common underlying anatomical irregularities in these two neurodevelopmental disorders. For example, the shared brain abnormalities between the ADHD and ASD groups of an increase in grey matter in the left inferior parietal/postcentral gyrus may underlie shared cognitive deficits in these groups, such as response inhibition in the absence of repetitive cues. The executive dysfunction theories of autism and ADHD hold that deficits in executive function account for the defining behavioural features of these two disorders. Both children with ADHD and children with autism show deficits in verbal fluency, and spatial working memory. A deficit in response inhibition is consistently reported in ADHD, and a number of studies have also described impaired response inhibition in autism.

Conclusions: most studies suggesting co-occurrence of ADHD and ASD have been based on relatively small and highly selected clinical samples, which can be prone to referral bias and failed to address other possible artifacts in the detection of co-morbidity. A heterogeneous approach to defining psychiatric co-morbidity was observed. In order to determine whether symptoms of ADHD and autism naturally cluster in children from the general population, it is important to examine these associations in larger, population-based samples using best possible methods.

112.19 19 Differential or Co-Morbid Diagnoses? Asperger's Disorder and PTSD in a Pre-Schooler. A. Bernard*[1], B. Siegel[2] and E. Marco[1], (1)*UC San Francisco*, (2)*University of California, San Francisco*

Background:

To date, there exist few empirical or anecdotal studies of individuals with autism spectrum disorders (ASD) presenting with posttraumatic stress disorder (PTSD). The deficits associated with ASD may make this population especially susceptible to traumatic experiences. Autistic individuals frequently present with an inability to read social cues including gesture, affect and body language. Caregivers may interpret their non-comprehension as defiance. They are often living in group care, they may not be able to communicate their experiences effectively, and their ASD diagnoses may overshadow the significance of other symptoms. Most importantly, the dearth of literature about co-morbid diagnoses results in a lack of professional knowledge about how to recognize, diagnose and treat PTSD in autistic individuals.

Objectives:

We present a case of co-morbid ASD and PTSD in PL, a 4 year old male with retinoblastoma since age 9 months. The goal of this case study is to add to the literature about PTSD diagnoses in the

ASD population, consider overlapping behaviors in differential diagnoses, and invite discussion about how best to diagnose and treat similar cases moving forward.

Methods:

Evaluations of PL included:

1) 3.1 years: Comprehensive diagnostic interview and cognitive evaluation to assess ASD and PTSD

2) 4.2 years: Diagnostic re-assessment while still in cancer treatment

3) 4.7 years: Follow-up assessment including ADOS and ADI-R following ASD intervention and cancer remission

Results:

3.1: PL was diagnosed with PDD-NOS based on language delay, social impairment, and a questionable preoccupation with letters and numbers.

4.2: PL met criteria for Asperger's disorder and PTSD secondary to repeated monthly invasive procedures consisting of general anesthesia followed by two days of complete eye bandaging. PL expressed resultant anxiety by naming areas of his home after city intersections and avoiding the area named for the hospital address. The symptoms were chronic and characterized by flattened affect punctuated by irritability, outbursts of anger and hypervigilance. His avoidance of the "map" locations fulfilled the ASD criteria for non-functional routines and rituals. There was also a repetitive element as PL ceaselessly drew accurate maps of various parts of the world (particularly the Balkan States and Eurasia) and labeled walls of the examination room with city intersections. PL could read fluently and perform basic math. His social and communication deficiencies stood in great contrast to his non-verbal cognitive ability.

4.7: PL is in remission and enduring fewer invasive procedures. He receives regular therapy and music lessons which contribute to a predictable weekly schedule. His PTSD symptoms are significantly diminished; he no longer perseverates on maps or avoids areas of his home. Scores on the ADI-R and ADOS indicate ASD, though the clinical impression is that his social engagement, interests, verbal and non-verbal communication have all improved. The most marked remaining deficits are atypical social initiation, stereotyped speech, and failure to develop peer relationships.

Conclusions:

With little empirical research to address the interplay of PSTD and ASD, clinicians face limited diagnostic and treatment precedent. We will present a model for characterizing differential diagnoses and co-morbidity of these disorders.

112.20 20 Can CBCL/1.5-5 Distinguish Between Autism and Attention Deficit Disorder?. L. Albores-Gallo*[1], L. Hernández-Guzmán[2], J. A. Díaz-Pichardo[1], B. Cortes-Hernández[1] and C. Hasfura-Buenaga[1], (1)*Hospital Psiquiátrico Infantil Dr. Juan N. Navarro. Secretaria de Salud*, (2)*Universidad Nacional Autónoma de México*

Background:

Autistic Spectrum Disorders (ASD) and Attention-Deficit /Hyperactivity Disorder (ADHD) are common neuropsychiatry syndromes which begin in childhood. Attention problems have been described in autism. Some authors report that 60% of children with Pervasive Developmental Disorder (PDD) meet criteria for ADHD. In contrast, autistic traits have also been identified in children with ADHD. Misdiagnosis is very common, in a recent study 33% of children classified as ADHD when assessed with the ADI-R were rediagnosed as PDD. Recent studies confirm that the most common diagnosis prior to autism is ADHD. Current DSM-IV exclusion criteria makes impossible to make a dual diagnosis (ADHD + Autism) in children.

The CBCL/1.5-5 is a parent-report checklist designed for assessing most frequent emotional and behavioral problems of children between 18 months through 5 years old. DSM-oriented scales have been added to empirically based scales which include: Affective, Anxiety, ADHD, Oppositional Defiant, and PDD Problems.

Objectives:

To examine if the CBCL/1.5-5/PDD and Attention-problems subscales can discriminate children with Autism versus ADHD and a healthy control group (HC).

Methods:

A total of 438 parents of preschool children with a mean age of 4.4±1.1 participated in the study from two different settings. The community sample consisted of 376 children recruited through 6 nurseries. The clinical sample consisted of 62 patients seeking attention in the Psychiatric Hospital Dr. Juan N. Navarro. Parents in both groups completed the CBCL/1.5-5, the response rate was 80%, the mother being the most frequent informant (77.6%). The clinical group was assessed through observation with appropriate play materials and their parents completed structured interviews to assign a DSM-IV diagnosis of Autism, Asperger, PDDNOS, ADHD and Other Psychiatric Diagnosis. ROC curves were used to determine criterion validity for the CBCL/1.5-5-PDD. Sensitivity and specificity for different cutoff points were calculated for assessing ASD group from either HC or ADHD. Mean differences were used to test if the CBCL/1.5-5/Attention problems and ADHD subscales could distinguish autism versus ADHD groups.

Results:

The ASD group had the highest ratings in the CBCL/1.5-5/PDD ($p<.001$) in contrast to the ADHD and the OPD group. However, the autism group had lower ratings than the Asperger group (11.6 vs.13.5) despite autism is considered as a more severe disorder. Elevated punctuations for the ASD group on the CBCL/1.5-5/ADHD and attention problems subscales could not differentiate them from the ADHD group. Roc curves show that the PDD subscale could effectively distinguish PDD vs. Healthy and ASD vs. ADHD (AUC of .95 to .97). The CBCL/1.5-5-PDD showed excellent sensitivity and specificity through ROC curves in differentiating children with ASD from either healthy controls or with ADHD. The CBCL/1.5-5/Attention problems and ADHD- subscales fail to discriminate the groups.

Conclusions:

Given the high co-morbidity between autism and ADHD, resulting in common misdiagnosis, children should be evaluated with instruments that assess for both, autism and ADHD to avoid misclassification which leads to inaccurate and incomplete psychiatric and psychosocial treatment. The CBCL/1.5-5 can be used to identify children with developmental problems as a first screening measure for clinical or epidemiology studies.

112.21 21 Co-Occurrence of Autism Spectrum Disorders in Individuals with Gender Dysphoria. I. L. J. Noens*[1], A. L. C. de Vries[2], P. T. Cohen-Kettenis[2], T. A. H. Doreleijers[2] and I. A. van Berckelaer-Onnes[3], (1)*Katholieke Universiteit Leuven*, (2)*VU University Medical Center*, (3)*Leiden University*

Background: Clinical experience suggests that the co-occurrence of gender dysphoria and autism spectrum disorders (ASD) is not a rare phenomenon; it occurs more frequently than one would expect by chance. To date, however, only case studies have been published and authors have very different views on how to understand the co-existence of ASD and gender dysphoria.

Objectives: This study seeks (1) to examine the incidence of ASD in individuals with gender dysphoria in a gender identity clinic, and (2) to gain more insight in the relation between ASD and gender dysphoria.

Methods: From April 2004 to December 2007, all children and adolescents referred to the Amsterdam Gender Identity Clinic were screened for ASD features. Referred individuals received a standardized clinical evaluation, consisting of a psychodiagnostic assessment, interviews with the child or adolescents, interviews with the parents about developmental history and current functioning, and information from the teacher. When an ASD was either suspected or previously diagnosed, the Dutch version of the Diagnostic Interview for Social and Communication Disorders-10th revision (DISCO-10; Wing, 1999; Dutch version: van Berckelaer-Onnes et al., 2003) was administered from the caregivers. In addition, the DISCO-10 was administered from the caregivers of seven young adults (all males, age 19-25) who were referred to the gender identity clinic and either had a histery of ASD or were suspected to suffer from ASD.

Results: Preliminary results indicate that at least 6 % of the 233 referred children and adolescents has an ASD. This percentage remains almost the same for the referrals with a confirmed Gender Idenity Disorder (GID) or Gender Identity Disorder-Not Otherwise Specified (GID-NOS) diagnosis. The group of individuals with ASD and GID (seven adults included) is heterogeneous in various respects: sex (both male and female), GID classification (GID, GID-NOS, transvestic fetishism), ASD classification (AD, Asperger

syndrome, PDD-NOS), age of onset of GID (before or after puberty), and developmental trajectory (cross-sex behavior temporary or persistent).

Conclusions: The results of this study indicate clearly that the co-occurence of ASD and gender dysphoria is a frequent occasion. The developmental trajectories of individuals with ASD and GID very considerably and thus require a differentiated clinical approach.

112.22 22 Motor Abilites of Children with FXS with and without Autism: Implications for Intervention. C. Zingerevich*[1], L. Greiss-Hess[2], K. Lemons-Chitwood[2], S. W. Harris[2], D. Hessl[2] and R. Hagerman[3], (1)*Rady Children's Hospital*, (2)*M.I.N.D. Institute, University of California at Davis Medical Center*, (3)*UC Davis*

Background: Previous studies suggested that children diagnosed with fragile X syndrome (FXS) often meet criteria for autism or PDD.

Objectives: The purpose of this study is to describe the motor abilities of children diagnosed with FXS with and without autism, and to compare the motor scores of these two groups controlling for cognitive level.

Methods: Forty-eight children, ages 12–76 months (SD = 16) diagnosed with FXS were assessed with the Mullen Scales of Early Learning, and the Autism Diagnostic Observation Schedule. Their parents were interviewed with the Autism Diagnostic Interview-Revised. We used a one-way analysis of variance to determine if the fine motor scale of the Mullen would show group differences based on autism classifications for the sample. In addition, we used Pearson correlation coefficient to examine the relationship between the cognitive level, the autism severity and the motor abilities. Lastly, we conducted a one-way analysis of covariance to determine the difference between the motor abilities of the Autism Spectrum Disorder groups controlling for cognitive level.

Results: We found that 60% of the children with FXS met criteria for autism or Pervasive Developmental Disorder – Not otherwise specified (PDD-NOS). Children with FXS with autism and PDD-NOS had lower fine motor scores than those without. However, there was no significant association between degree of motor impairment and communication and social impairments after controlling for cognitive level, indicating that cognitive level contributes to impaired motor abilities of children diagnosed with FXS and autism, more than the severity of autism symptoms.

Conclusions: Children with FXS and autism are at risk for impaired motor abilities. Implications for development and intervention are discussed.

112.23 23 Quantitative and Qualitative Assessment of Diadochokinesia in Autism Spectrum Disorders. L. Ruta*[1], F. Taffoni[2], L. Mazzone[1], N. Russo[1], D. Campolo[2], E. Guglielmelli[2] and F. Keller[3], (1)*University of Catania, Italy*, (2)*Lab.of Biomedical Robotics & Bio-Microsystem*, (3)*Università Campus Bio-Medico di Roma*

Background: Cerebellar abnormalities, with Purkinje neuron loss and impaired diadochokinesis as well as poor praxis performances have been reported in ASC.
Objectives: (1) to assess diadochokinesis, coordination skills and motor processing abilities in typically developing children (CG) and children diagnosed with ASC (High Functioning Autism and Asperger Syndrome), through the use of magneto-inertial devices (XSens MTx, XSens Motion Technologies®) applied to both wrists. (2) to evaluate the possible correlations between diagnosis, laterality, autistic traits and kinematic indexes.
Methods: 31 consecutive subjects (15 ASC; 16 CG) aged 5-14 years and matched for age, gender and IQ were compared. The Edinburgh Handedness Inventory assessed the lateral preference. The children version of the Autism-spectrum Quotient (AQ-Child), validated in Italian, was administered for quantifying the number of autistic traits, in a continuum of severity. The Total score (0-150) and the sub-scores in five different domains (Social Skills, Attention Switching, Attention to detail, Communication and Imagination) were rated. The kinematic analysis was conducted recording the prono-supination at the wrist joints at maximal and comfortable velocity respectively and after a trigger acoustic stimulus at five different frequencies from 1 to 5Hz. A real time visual feedback (in form of a 3-D cube on a computer screen, representing the orientation of one wrist) was given to the child in order to make the test more appealing. The following motor variables and indices were considered: (1) Prono-supination range (maximal angular excursion during the movement); (2) Prono-supination frequency (the inverse of the mean period of a complete prono-supination movements); (3) Main Prono-supination axis (the mean orientation of the axis around which the

pronosupination movement takes place); (4) Inter-axes angle (the angle between the two main prono-supination axes); (5) Delay of one hand related to the other.
Results: Preliminary data analysis showed: (1) a statistical significant difference between ASC and CG in the AQ-Child total score and Social Skills, Attention Switching, Communication and Imagination sub-scores. (2) a significant positive correlation between right-handedness and the Main Prono-supination axis at 3 Hz. (3) a significant positive correlation between: (a) the AQ-Child (total score and Social Skills subscores) and the Prono-supination range at 2 Hz (b) the AQ-Child (total score and Social Skills, Communication, Imagination and Attention Switching subscores) and the Prono-supination frequency at 1 Hz. (4) a significant negative correlation between the AQ-Child (total, Imagination and Attention to detail scores) and the Prono-supination range at 5 Hz. (5) a significant negative correlation between right-handedness and the Inter-axes angle at 3 Hz, the Prono-supination range at 5 Hz and the Prono-supination frequency both right and left at 2-3 Hz.
Conclusions: Preliminary data analysis displayed a statistical significant difference between ASC and CG in the AQ-Child, with ASC group showing higher scores. The AQ scores also correlated with the kinematic indexes. In particular, at higher frequencies (5Hz) the AQ positively correlated with a worse performance. Further analyses are needed to better clarify the potentially peculiar patterns of motor impairment and dyspraxia in ASC.

112.24 24 Motor Stereotypies in Autism and Rett Syndrome:Difference and Similarities. S. Goldman*[1] and T. Temudo[2], (1)*Albert Einstein College of Medicine*, (2)*Hospital Santo António*

Background: Rett Syndrome (RS) and Autistic Disorder (AD) share many phenotypic features, one of them stereotypies, defined as repetitive, rhythmical, patterned, purposeless movements like hand flapping**.** Our previous research showed that, in addition to their signature hand-washing stereotypies, girls with RS have many others, some overlapping those of children with AD. The neurologic basis of stereotypies is poorly understood, even in RS despite its known genetic basis.

Objectives: Our goal is detailed description and comparison of the motor stereotypies of AD and RS, hoping to advance understanding of their pathophysiology and management. Our first step was to detail similarities and differences in the frequency, topography, and variety of stereotypies which might provide clues to their underlying circuitry. The second was to determine whether specific stereotypies, besides the signature hand stereotypies of RS, characterize one or the other disorder and thus may help early diagnosis.

Methods: Twenty girls with RS recruited in Portugal were videotaped during a neurologic examination. All had *MECP2* mutations and NVIQs < 70; 9 could walk independently. Mean chronologic age was 60 months (range 36-96). Twenty American children (11 boys, 9 girls) with AD were matched for chronological age and NVIQ (mean age 68 months, range 33-98). Our preliminary research found no influence of gender on stereotypies. All AD children underwent comprehensive behavioral and neurological evaluations, were ambulatory, and none had a frank neurologic disorder. They were videotaped during a standardized play session. In both groups the 5 minute video segment selected for scoring of each stereotypy was the most representative of that child. Coding included frequency, variety, and body parts affected with particular attention to the hands. Significance was set at $p<0.05$

Results: Stereotypies were continuous in half the children with RS (50% vs.15% in AD). Stereotypies were infrequent (at most 2 during 5 minutes) in 35% of children with AD (5% in RS). All hand stereotypies in RS children were midline, compared to 30% in AD. Stereotypies with hands together (e.g., "washing," clapping, clenching) characterized RS (60%) rather than AD (10%). Hand to mouth or to face was also more prevalent in RS (65% vs.15%). Fewer stereotypies in RS girls with sufficient hand use involved an object (30% vs. 60%). There was no difference between groups in rocking, stereotypic gaits (RS girls able to walk), variety, complexity, or dystonic features of the stereotypies.

Conclusions: The neurologic origin of RS stereotypies is taken for granted whereas it remains controversial in AD, despite strong overlaps between them. Useful differences in RS include their quasi-continuousness, the signature involvement of joined hands in the midline, and frequent touching of mouth and face. Compulsive perseverative use of objects points to AD and

suggests orbitofronto-striato-thalamo-cortical circuitry rather than a more strongly subcortical basis for the more elementary movements in RS. Recent animal and human research suggests that stereotypies may denote reversible dysfunction rather than fixed damage in both. Advanced imaging will be required to help resolve these differences which may have important implications for future pharmacologic management.

112.25 25 Movement in Infants with Autism Spectrum Disorder: The Analysis of Motor Milestones in Infancy. P. Venuti*, G. Esposito and S. deFalco, *University of Trento*

Background: Early identification of children with autism spectrum disorders (ASD) has recognized as a critical aspect of their medical management and treatment. Movement disorders are considered one of the first signs which probably precede social or linguistic abnormalities.

Objectives: Our study aims to verify, through observational methods, the possibility of distinguishing infants with ASD from infants with typical development (TD) or with developmental delay (DD) by movement.

Methods: the Eshkol-Wachman Movement Analysis System which analyses static and dynamical symmetry during lying, sitting, standing and walking was applied to 161 retrospective home videos of children (ASD=58; TD=58; DD=45) during the first two years of life.

Results: data shows significant differences between ASD and the two control groups ($p<.05$). Our data also highlight differences within ASD group, revealing two types of ASD infants characterised by high or low levels of symmetry.

Conclusions: movement disorders can be considered as a possible sign in early diagnosis of ASD. We suggest that different pattern of motor functioning probably relate to different pathways to ASD. We hypothesise that the low levels of symmetry since the first months of life could be related to the loss of the Purkinje cells described in ASD.

112.26 26 Children with Autism Show Excessive Reliance on Proprioception in Building Internal Models of Action. C. C. Haswell*[1], J. Izawa[1], S. H. Mostofsky[2] and R. Shadmehr[1], (1)*Johns Hopkins University*, (2)*Kennedy Krieger Institute, Johns Hopkins University School of Medicine*

Background:
Children with autism exhibit motor dysfunctions including poor coordination and difficulty with performing/imitating skilled gestures. One of the crucial steps in motor learning is for the brain to form internal models: a mapping between motor commands and the expected visual and proprioceptive sensory feedback. These internal models are the basis for which the brain understands actions of others. However, it is not clear yet how the neural mechanism of internal model is disordered in the autistic brain.
Objectives:
In order to understand a mechanism of the motor disorder in the autistic brain, we examined the differences of the neural representation of internal model between high functioning children with autism (HFA) and typically developing children (TD). If the internal model is a mapping between motor commands and visual sensory feedback, the skill generalizes in Cartesian coordinates; whereas, if it were formed on proprioceptive space, the memory would generalize in the intrinsic coordinates of joints and muscles. The objective of the study was to quantify the property of the generalization of learning of internal model by examining how the learned motor memory could transfer to generalize across arm posture.
Methods:
HFA and TD children performed a reaching task that involved learning an internal model of a novel tool (a robotic arm). Subjects were trained to reach to the forward direction in left workspace while holding a robotic arm; the robotic arm produced a curl force field so that subjects had to learn to adapt their movements to hit the target. Learning was then tested in the left, as well as the right, workspace using a channel that clamped the trajectory error so that the force that the subject produced to compensate the applied force was measured. Generalization of learning to the right workspace was assessed using two directions: one required production of the identical movement in Cartesian (visually-based) coordinates and the other required the movement to be produced in joint coordinates.
Results:
Both HFA and TD adapted to the force similarly ($F(1,408)=0.892$, $p=0.3543$). We found the learning generalized in joint coordinates for both HFA and TD. This supports the results in our previous study, which suggests that an internal model relies on an association between proprioception and muscle forces. The new finding here is that HFA generalized in joint coordinates

to significantly larger extent than TD ($F(1,408)=8.91$, $p=0.0064$).
Conclusions:
More generalization in joint coordinates implies that in learning an internal model of self generated action, the HFA brain builds a stronger than normal association between motor commands and proprioceptive feedback. Because the action perception involves information transformation between the visual feedback and the motor command, the larger than normal reliance on proprioception may explain deficits in action perception in HFA. Furthermore, because the brain of autistic children shows an overgrowth of localized white matter connections, it is possible that this abnormally strong association between motor commands and proprioception in HFA is a correlate of this anatomical feature.

112.27 27 Motor Performance in Young Children with An Autism Spectrum Disorder. S. Tomchek*, *Weisskopf Child Evaluation Center*

Background: In comparison to language and social skill, individuals with an ASD have been described as having better basic motor skills. The timing and sequence of motor developmental markers have, however, been described as both delayed and qualitatively different in individuals with ASDs than that of typically developing children. Further deficits with motor planning have also been identified.

Objectives: The purpose of this study was to describe the motor performance skills of a large sample of children with an ASD and compare with other developmental measures.

Methods: Retrospective collection was used to gather data on 400 individuals between 3 and 6 years of age diagnosed with an ASD during a comprehensive diagnostic team evaluation at a diagnostic center specializing in autism. Each participant received a comprehensive developmental medical, psychological, speech and language, and occupational therapy evaluation. The resultant developmental adaptive, social, communication, and motor variables yielded from this evaluation process were analyzed. Consistent measures for all variables across subjects or cross-validation of measures was employed. The primary motor variables were Gross Motor (GMQ) and Fine-Motor Quotients (FMQ) from the *Peabody Developmental Motor Scales First* (Folio & Fewell, 1983) *or Second Edition* (Folio & Fewell, 2000). Additional qualitative indicators of muscle tone, strength, balance, stability, and handedness were also collected for descriptive analysis and measurement of consistency between developmental medicine and occupational therapy.

Results: The majority of the subjects demonstrated adequate strength, though presented with muscular hypotonia and delayed onset of handedness. Although, motor skills (both gross and fine) were statistically and consistently higher than other developmental variables (language, social, adaptive), significant delays of 2 standard deviations were noted for 86.3% of the sample in gross motor skill and 88.8% for fine motor skill. Group differences were noted by diagnosis with lower gross motor quotients noted in the autism group when compared to PDD-NOS and Asperger groups. The Asperger group demonstrated higher fine motor quotient scores than both Autism and PDD-NOS groups. Regarding age differences, significant FMQ differences between the 3-year-old and 4- year-old subject groups and the 3 year old and 5 year old groups, with higher 3 year old quotient scores noted than both 4 and 5 year old groups. No age differences were noted for gross motor quotient scores.

Conclusions: Findings are consistent with previous reports of motor performance. Motor performance deficits are demonstrated in this large sample of preschool-aged children with an autism spectrum disorder. These motor impairments likely contribute to functional limitations in play and adaptive performance. Further research providing a better understanding of motor aspects unique to the diagnosis may have implications for understanding neurological underpinnings, early diagnosis, and guide treatment programs.

112.28 28 Examination of Motor Sequence Learning Over Multiple Sessions in Children with Autism. S. Spinelli*[1], L. R. Dowell[1] and S. H. Mostofsky[2], (1)*Kennedy Krieger Institute*, (2)*Kennedy Krieger Institute, Johns Hopkins University School of Medicine*

Background: Autism is a developmental disorder characterized by abnormalities in the acquisition of social, communicative and motor skills. Given the developmental context of autism spectrum disorders, careful examination of mechanisms underlying learning and memory may be critical to understanding the neural basis of autism and to refining treatment. Motor sequence and other

forms of procedural learning have thus far been examined in autism over a single session. However, acquisition of skill through procedural means tends to be a gradual process that results in acquisition of skills that are very stable over time.

Objectives: To examine motor sequence learning in children with high-functioning autism (HFA) over the course of multiple sessions.

Methods: 5 children with HFA and typically developing (TD) 5 children completed a Rotary Pursuit (RP) task over two consecutive days with two sessions a day (sessions 1 to 4). Each session consisted of four blocks and each block consisted of three 30-second trails. Improving performance on the RP task involves learning a sequence of complex movements that anticipate the motion of a target in a novel pattern. Each subject performed one of two motor patterns (either circle or square), with the first session of day 2 (session 3, block 3) also including a single interference block, so that children performing the circle pattern were exposed to a block of square trails and children performing the pattern square pattern were exposed to a block of circle trials. For both experiments, learning was assessed using repeated measures ANOVA (RM-ANOVA) to examine change in time-on-target across blocks.

Results: Analysis across all sessions revealed a significant main effect of diagnosis ($F_{1,8}=6.9$, $p<0.03$), with children with HFA showing less overall time-on-target than did TD children. Across both groups, there was a significant main effect of sessions ($F_{3,24}=4.6$, $p<0.02$), with an increase in time-on-target Both groups showed increased performance over blocks and sessions, however children with HFA showed less time on target than TD children in all the 4 sessions. Analysis of the interference effect in session 3 (change from block 2 to 3) revealed that while TD children showed a near significant decrease in time-on-target ($F_{1,5}=4.6$ $p=0.08$), children with HFA ($p>0.2$) did not.

Conclusions: The RP findings over multiple sessions indicated that while children with autism showed less time-on-target than do TD children, both groups showed improved performance consistent with motor learning. There is suggestion, however, that for children with autism the mechanism used to acquire the motor sequence may have differed from TD children; children with HFA showed show less decrement in performance during the interference block compared to TD children. The lesser interference effect of a contrary visual pattern may be indicative of decreased reliance on visual feedback to guide acquisition of novel sequences of movement. The findings have implications for therapies aimed at helping children with autism to acquire new skills, motor skills as well as aspects of social skills that depend on learning novel motor gestures.

112.29 29 Children with Autism Show Specific Handwriting Impairments. C. T. Fuentes*[1], S. H. Mostofsky[2] and A. J. Bastian[1], (1)*Johns Hopkins School of Medicine, Kennedy Krieger Institute*, (2)*Kennedy Krieger Institute, Johns Hopkins University School of Medicine*

Background: Handwriting skills, which are crucial for success in school, communication, and building children's self-esteem, are frequently poor in individuals with autism. Despite the importance of these skills and the frequency with which individuals with autism are found to be impaired, the only study specifically examining handwriting in this population focused on letter size in adults. No study has explored handwriting in children with autism, and no study has tried to tease apart the multiple aspects of handwriting that may differentially contribute to impairments in autism. As a result, the specific aspects of handwriting in which individuals with autism demonstrate difficulty remain unknown.

Objectives: We asked whether, consistent with common observations, children with high-functioning autism (HFA) show overall handwriting impairments. If so, we wanted to further assess whether these impairments are in specific qualitative categories that can be differentially addressed during training and whether the impairments can be accounted for by factors such as age, intelligence, visuospatial abilities, and motor abilities.

Methods: We studied handwriting samples from children between the ages of 8 and 12 with and without HFA by using the Minnesota Handwriting Assessment. Samples were scored by two experimenters on an individual letter basis, with each letter receiving a score in five qualitative categories: legibility, form, alignment, size, and spacing. Most qualitative scoring was based on ruler measurements, and additionally an overall rate score was obtained. Subjects were also tested on the Wechsler Intelligence Scale for Children IV

(WISC-IV) and the Physical and Neurological Examination for Subtle (Motor) Signs (PANESS).

Results: We demonstrated that children with HFA do indeed show overall worse performance on a handwriting task than do age- and IQ-matched controls. More specifically, children with HFA show worse quality of forming letters but do not show differences in their ability to correctly size, align, and space their letters. Among all subjects, PANESS scores were significantly predictive of legibility and form scores, whereas age and IQ (full-scale and sub-scores) were not.

Conclusions: We have provided the first systematic demonstration that children with HFA show overall worse handwriting performance relative to controls. Rather than showing random impairments, handwriting performance was specifically worse in the quality of form of letters while performance in other qualitative categories was comparable to controls. General motor abilities were a strong predictor of handwriting performance, as opposed to age, intelligence, and visuospatial abilities. These results suggest that training targeting letter formation, potentially in combination with compensatory motor strategies, may be the best direction for improving handwriting performance in children with autism.

112.30 30 The Effects of Learning to Ride a Two Wheeled Bicycle on Social Skill Development in Youth with Autism Spectrum Disorder. M. I. MacDonald* and D. A. Ulrich, *University of Michigan*

Background: Teaching age-appropriate social skills to children and youth with Autism Spectrum Disorder (ASD) is of particular importance. The wider the gap between a child with a social skill deficit and a child with age-appropriate social skills, the more quickly a child can be rejected amongst their peers. Although generalization is a primary goal of social skill intervention programs for youth with ASD, findings indicate the contrary; generalization is not occurring in 'real life' situations and because of this youth with ASD are missing out in reciprocal interactions with peers (Meier, 2006). The ability to ride a two-wheeled bicycle is considered a societal norm in (Klein, 2004). Most children learn how to ride a bicycle by the age of 6- 7 years. Since age-matched peers and structured activities tend to play a key role in the retention and generalization of social skills, physical activity seems to be an appropriate vehicle for this type of practice.

Objectives: This study aims to understand the impact that learning to ride a two-wheeled bicycle has on social skill development in youth with ASD.
Methods: Data for this study came from four parents of youth with ASD between the ages of 11-16 years old. All of the parents had a child who successfully learned to ride a two-wheeled bicycle in 5 days of training. Semi-structured interviews were used as a method of data collection. The interview questions addressed areas of social skill development occurring as a result of learning to ride a two-wheeled bicycle. Each interview was transcribed verbatim and open coded. Open codes resulted in 28 axial codes from which two primary themes emerged.
Results: The primary themes that emerged from the data indicted that the generalization of social skills and family and peer relationships were impacted upon because of the youth with ASD's ability to ride a two-wheeled bicycle. The generalization of social skills included more independence, confidence, communication and coping. Learning to ride a two-wheeled bicycle also had a positive impact on family relationships, but particularly sibling relationships. Parents indicated that obtaining the ability to ride a two-wheeled bicycle aided in creating an environment for family activities without making special accommodations for their youth with ASD. Peer relationships were significantly increased in two of youth participants based on their ability to ride a two-wheeled bicycle. Peer relationships consisted of positive changes including spending more time with age-matched peers and having the ability to participate in neighborhood riding activities with children of similar ages.
Conclusions: Learning an age-appropriate motor behavior, such as riding a two-wheeled bicycle is helpful in establishing an environment to enhance social skill generalization and peer and family relationships. Future research will involve randomized trials designed to teach youth with ASD how to ride a two-wheeled bicycle and monitor social skill generalization longitudinally.

112.31 31 Can We Teach Youth with ASD to Ride a Two Wheel Bicycle?. D. A. Ulrich*, M. I. MacDonald, P. M. Esposito, I. V. Jeong and J. L. Hauck, *University of Michigan*

Background: Research consistently indicates that youth with Autism Spectrum Disorders (ASD) display major constraints in acquiring an adequate repertoire of functional physical activities they can use with their family, siblings, and peers. Most of this research literature indicates that quality of life, health, and social interactions are negatively

impacted as a result of deficits in their physical activity. There has been an increase in the number of studies designed to describe physical activity patterns in a variety of children, youth, and adults with developmental disabilities but very few interventions have been tested to improve the amount of time spent in moderate to vigorous physical activity levels in youth with ASD. In 2005/ 2006, we conducted a randomized trial involving youth with Down syndrome (DS) where the experimental group received individualized bicycle training using the training protocol established by Lose the Training Wheels and the control group received the same training one year later. Our criterion for success in riding a two wheel bicycle in this initial study was that the rider had to demonstrate the ability to ride their bicycle more than 30 feet without support. Results from this randomized study indicated that 62% of children with DS aged 8-15 years succeeded in mastering the criterion following 5 days of training, 75 minutes per day.

Objectives: The purpose of this 2008 study was to successfully teach youth with ASD how to ride a two wheel bicycle.

Methods: This study was an extension of the 2005-2006 study. Success criterion was increased to more than 100 feet of continuous riding without support. We recruited higher-functioning youth with ASD in the age range of 9-18 years. The following exclusion criteria were pre-established: medical conditions that precluded moderate to vigorous physical activity (seizure disorders or heart conditions), obesity, and major behavior problems in new situations. Individualized training was implemented 75 minutes each day for 5 consecutive days.

Results: The following results were observed: 31 youth with ASD participated in the study. The average age of the riders with ASD was 11.9 years old (SD= 2.4). Successful riding was achieved by 71% of the sample. Of those who achieved the ability to ride, 86.4% could use their hand brake to stop and 90.9% could self start their bicycle. Recommendations for future research and practice will be discussed along with strategies to increase continued riding.

Conclusions: Learning to ride a two wheel bicycle independently is an achievable life time activity for youth with ASD. This activity should increase social interaction opportunities and participation in community activities, all of which have been reported as critical needs for this population. Future research is needed to document longitudinal outcomes through randomized clinical trials.

112.32 32 Movement Skill Performance by Children with Autism Spectrum Disorders: Delays, Deficits, and Developmental Trajectories. K. Staples* and G. Reid, *McGill University*

Background: The nature of ASD is integrally related to development given characteristic behaviours are evident early in life, pervade nearly every aspect of subsequent development, and continue to change throughout the course of development. Movement skills play a critical role in development and it is generally accepted that performance of movement skills by children with ASD is impaired compared to peers without ASD, suggesting possible delays in the development of movement skills. These movement skill differences seemingly become more obvious with increasing age, although ongoing debate exists whether these differences simply reflect delays or if development among children with ASD is in some ways unique and follows a different developmental trajectory than their typically developing peers.

Objectives: This study explored the performance of fundamental movement skills among 9 to 12 year old children with ASD using the *Test of Gross Motor Development* (*TGMD-2*), a criterion referenced assessment that provides a developmental framework to examine both locomotor and object control skills. A longitudinal design with two carefully planned comparison groups afforded a more detailed exploration of movement skill development through the notion of delays, deficits, and developmental trajectories.

Methods: The primary group of 26 children with ASD was individually-matched to two typically developing comparison groups. The first comparison group was matched on sex and chronological age, while the second group was matched on sex and the raw score from the locomotor portion of the *TGMD-2*. To explore trajectories of development, movement skill performance of 12 children with ASD and 15 children in the developmentally-matched comparison group was followed for 3 consecutive years.

Results: Comparison to the age-matched group confirmed expected performance differences on both locomotor and object control subtests of the *TGMD-2*. By definition, the developmentally-

matched group was younger, ages 4 to 6 years. Longitudinal comparison between these groups revealed different developmental trajectories. Despite being much older, children with ASD seemingly reached a plateau in the performance of both locomotor and object control skills, while the younger, typically developing children continued to refine their performance with increasing age.
Conclusions: The developmentally-matched comparison group clearly demonstrates a delay in the development of fundamental movement skills among children with ASD. The obvious age differences, extent of impairment resulting from cumulative delays, and increasing differences reflected in the developmental trajectories would suggest that children with ASD develop movement skills differently than their typically developing peers. Current teaching strategies and intervention approaches therefore need to reflect these unique patterns of development.

112.33 33 Assessment and Identification of Developmental Dyspraxia in ASD. H. Stieglitz Ham*[1], A. Bartolo[2], M. Corley[1], S. Swanson[3] and T. Rajendran[4], (1)*University of Edinburgh*, (2)*Universite' de Lille Nord de France*, (3)*Medical College of Wisconsin*, (4)*University of Strathclyde*

Background: Both developmental dyspraxia and acquired limb apraxia are disorders of gestural processing. However, in developmental studies, dyspraxia is often referred to as a 'unitary disorder', mainly affecting imitation abilities; whereas limb apraxia is usually described as a complex disease, affecting both the production and reception of gestures. To justify the complexity of limb apraxia, recent cognitive models of praxis processing have been devised (Rothi et al., 1991; Cubelli et al., 2000). These models enable the identification of specific patterns of deficits associated to praxis processing in patients with brain damage. Recent findings suggest that dyspraxia in individuals with autism might not be limited to imitation deficits (Mostofsky et al., 2006; Stieglitz Ham, Corley, Rajendran, Carletta, & Swanson, 2008). Therefore, only by employing a complete praxis assessment, as is done in studies of limb apraxia, is it possible to assess dyspraxia in autism in a more comprehensive manner.
Objectives: The aim of this study is to uncover specific praxis profiles in individuals with autism by means of a complete battery of tasks devised to evaluate the different cognitive mechanisms proposed by the cognitive model of praxis processig (Cubelli et al., 2000). Methods: 19 individuals with ASD entered this study. 23 TD controls were tested to gather norms. A battery of tasks has been entirely devised. For the evaluation of the integrity of the lexical route (Cubelli et al., 2000), six tasks assessed the ability to discriminate and comprehend meaningful gestures (transitive, intransitive and pantomimes), and five tasks assessed the ability to produce meaningful gestures across multiple modalities (verbal and visual for pantomimes and intransitive gestures; as well as actual object use. The evaluation of the non-lexical route was carried out with four tasks testing the imitation of meaningful and meaningless gestures. Gesture production was videotaped and coded by two examiners.
Results: Data showed that individuals with autism demonstrated specific patterns of praxis processing. With reference to the cognitive model of praxis processing usually employed in adult lesion patients, results uncovered individuals with ideational dyspraxia (n= 6) of ideomotor *dys*apraxia (n=4); and of ideational with ideomotor *dys*praxia (n=2) as well as individuals with deficits in imitation only (n = 2).
Conclusions: In summary, the cognitive model of praxis processing was useful in identifying specific patterns of praxis processing in individuals with autism

112.34 34 Sensory-Motor Deficits and Poor Independence : Prevalent Difficulties Not Unique to ASD. M. Couture*[1], E. Gisel[2], G. Reid[2] and E. Fombonne[2], (1)*Laval University*, (2)*McGill University*

Background: In recent years, the sensory-motor domain has gained increased attention among autism researchers. However, very few are addressing its impact on the autonomy or functional independence of children with autism spectrum disorders (ASD). Objectives: 1) To describe the sensory-motor deficits that are specific to preschool and school-aged children with ASD. 2) To compare the sensory-motor skills of the two age groups with selected clinical control groups and children with typical development. 3) To establish the contribution of sensory-motor skills to the functional independence in daily living skills of children with ASD. Methods: This is a clinical descriptive study of 154 children aged 3 to 11 years. Eighty-five (85) children with ASD, 34 with Typical Development (TD), and 37 with Developmental Disabilities such as Intellectual Disability (ID) or Speech Language Impairment (SLI) were recruited. Children were separated in two age groups: 95 preschoolers (3 to 5 y 11m)

and 59 school-aged (6 to 11) and were tested with the Peabody Developmental Motor Scales-PDMS-2 or the Movement ABC, the Sensory Profile, the Wee-FIM and the Vineland Adaptive Behavior Scales-VABS-2. Results: Cognitive performance (IQ) of each group of preschoolers was ASD = 61, DD = 68 and TD = 107; the performance of the school-aged groups was ASD = 76, DD = 53, and TD = 105. Sixty-six percent of preschoolers with ASD had abnormal sensory processing skills compared to 47% of children with DD and 20% of children with TD ($p < .05$). In contrast, 93% of school-aged children with ASD, 63% of children with DD and 25% of children with TD had abnormal sensory processing skills. On the motor performance of the PDMS-2, preschool children with ASD scored at the 4th centile of total motor performance, children with DD were at the 22nd and the TD group at the 46th centile. On the MABC, school-aged children with ASD scored at the 8th centile for total motor impairment, children with DD scored at the 3rd centile and the TD group scored at the 68th centile. Scores for the functional independence of Daily Living Skills on the VABS-2 were: preschoolers ASD : 76, DD : 83, TD : 104; school-aged children with ASD : 80, DD : 75, TD : 95. Regression analyses were conducted to identify predictive variables of autonomy and functional independence on the Wee-FIM and VABS-2. The best predictors for personal skills (DLS) were fine motor and sensory processing skills; they explained nearly 30 (ASD preschoolers) to 46% (ASD school-age) of the variance. Conclusions: Most children with ASD have some sensory-motor deficits; these do not disappear with age but rather seem to get exacerbated. Self-care skills as well as daily living skills of children with ASD and other developmental disabilities are very poor and will require support. Sensory-motor issues are not unique to ASD and should be addressed in all clinical populations, especially ID, presenting such difficulties. Interventions specifically targeting sensory processing and motor skills may lead to greater independence in self-care skills in children with ASD or other developmental disabilities. This study was conducted as part of a post-doctoral fellowship at the Montreal Children's Hospital of McGill University by the first author and was sponsored by the Canadian Child Health Clinician Scientist Program (CCHCSP) and the Autism Research Training (ART) program. Both are training grant initiatives of the Canadian Institutes of Health Research (CIHR).

112.35 35 Dysmorphic Features and Development of Children with Infantile Autism. P. Gorczyca*, A. Kapinos-Gorczyca and R. Hese, *Medical University of Silesia*

Background: Childhood autism is a neurodevelopmental disorder that is characterized by impairments in social interactions, verbal and non-verbal communication and a pattern of stereotypical behaviours and interests. The present theories suggest that autism is caused by the effects of genes and neurobiological factors. Numerous authors described certain dysmorphic features, commonly occurring separately in autistic persons. These features are considered to be the potential indicator of early neurodevelopmental disorders.

Objectives: The aim of the study was to establish the dysmorphic features of the face in a group of autistic children and to compare the results to a group with Asperger syndrome.

Methods: We examined 30 children with childhood autism and 30 with Asperger syndrome. Criteria DSM-IV and Childhood Autism Rating Scale (CARS) were used in diagnosis. The photoanthropometric method followed the protocol established by Stengel-Rutkowski et al. Parents were asked additionally to complete the Diagnostic Checklist for Behavior-Disturbed Children. Statistical analysis was conducted with the use of ANOVA Kruskal-Wallis and U Mann (**-)** Whitney tests, correlation analysis was made using χ^2 test and Spearmann index.

Results: Dysmorphies of the ear as well as nose were found in the group of autistic children. In the examined group there was the correlation between the amount of dysmorphies and the presence of some somatic disorders in the first-degree relatives. The presence of these disorders showed also the connection with the scores in Childhood Autism Rating Scale (CARS). Besides there was a relationship between the amount of dysmorphies and the motor development of autistic children.

Conclusions: In the patients with childhood autism the anteriorly rotated ears and the long back of the nose appeared more often. These parameters may become useful for early detection.

112.36 36 Autism: Developing Best Practice in Medication Use and Support Prior to Health Care Visits. J. Reinhold*, G. Klayman, J. Hansen and C. Verow, *Cincinnati Children's Hospital Medical Center*

Background:

Children with autism often have difficulty cooperating for health care visits. These difficulties are related to anxiety, sensory deficits, limited communication skills and inability to adapt to change. Trauma and mistrust of providers has resulted when patients are managed in a rushed manner with physical restraint. This occurs as the result of inadequate preparation of families and staff. Evidence-based practice statements do not exist to address best practice regarding preparation and the use of medication in children with autism prior to health care visits.

Objectives:

To propose that best practice includes preparing children with autism, families and staff prior to health care visits in order to improve the experience of care.

To develop an evidence-based best practice statement regarding the use of anti-anxiety medication prior to health care visits for children with autism.

Methods:

Child life staff developed a collaborative approach in supporting patients with autism and their families during health care visits. This collaboration included the medical team and a review of the appropriateness of using anti-anxiety medication prior to the visits. Preparation of the children and families involved assessment of the child's status, past experiences in health care settings, and ability to cope. Support interventions included: pre-visit preparation, alternative focus, adaptive use of communication tools, and other individualized efforts. Anti-anxiety medication was prescribed after assessment of the patient's anxiety level and likelihood of compliance with demands of the health care visit. A plan of care was established and appropriate interventions were provided during the health care visit to support the patient. The outcome of these visits was noted in the patient record and future recommendations were reviewed. A multidisciplinary staff/parent committee developed a best practice statement regarding the use of anti-anxiety medication, using an evidence-based approach, critiquing the scientific literature and current practice.

Results: The evidence-based best practice statement provides information about the safe use of anti-anxiety agents found to be helpful for those with autism who are presenting for health care visits. The objectives of health care visits were successfully accomplished with minimal patient trauma or distress. Barriers to preventive care were decreased and compliance for return visits dramatically increased. Staff productivity improved. Family satisfaction dramatically improved.

Conclusions: In keeping with the principles of family-centered care and best practice, this collaborative model changes the outcome in the delivery of essential health care services for those with autism. Best practice statements which address an evidence-based approach in the use of anti-anxiety medication improve safe and successful delivery of care. With this collaborative model, psychological sequelae and trauma are dramatically reduced and compliance for return visits is enhanced. Health care providers are obligated to develop individualized care approaches that incorporate adequate preparation, assess medication needs, and provide education. Successful patient/family outcomes are dependent upon mutual family/patient/staff collaboration. Lessening barriers and improving access to services, will potentially result in more positive long term health benefits for these individuals.

112.37 37 The Prevalence of Obesity in Children with Autism: a Secondary Data Analysis Using Nationally Representative Data from the National Survey of Children's Health. C. Curtin*[1], S. E. Anderson[2], A. Must[3] and L. Bandini[1], (1)*University of Massachusetts Medical School*, (2)*The Ohio State University*, (3)*Tufts University School of Medicine*

Background: The prevalence of childhood obesity has increased dramatically in the last two decades. Numerous efforts are underway to understand, prevent and intervene on this significant risk to children's health in typically developing children. However, little research has been done to assess the prevalence of obesity and risk factors associated with obesity in children with autism, a population that may be particularly vulnerable to the development of obesity by virtue of complex behavioral, physical, and psychosocial difficulties they experience. Understanding the prevalence of obesity in children with autism is an important undertaking, as it has implications for

overall health and wellbeing.
Objectives: The goal of the current study was to estimate the prevalence of obesity in children and adolescents with autism.
Methods: This study was a secondary data analysis of cross-sectional nationally representative data collected by telephone interview of parents/guardians on 85,272 children ages 3-17 from the 2003–2004 National Survey of Children's Health (NSCH). Autism was determined by response to the question, "Has a doctor or health professional ever told you that your child has autism?" Children and adolescents were classified as underweight, normal weight, overweight, or obese according to CDC guidelines (2000) for body mass index (BMI) for age and sex. **Results:** After adjustment for age, sex, race/ethnicity, and household income-to-poverty ratio, children and adolescents with autism were 20% more likely than children and adolescents without autism to be obese (odds ratio (OR) = 1.2, 95% CI = 0.8, 1.8).
Conclusions: This study suggests that children with autism have a prevalence of obesity at least as high as children overall. Standard public health approaches to obesity prevention may not meet the needs of this population of children, underscoring the need for additional research to understand better the factors that influence the development of obesity in children with autism.

112.38 38 Zinc in Autism: a Case-Control Study. A. Hagen*[1], E. Dewailly[2] and E. Fombonne[3], (1)*Montreal Children's Hospital*, (2)*Laval University Medical Center*, (3)*McGill University*

Background: Zinc supplementation is sometimes advocated to manage autism despite a paucity of research evidence on this topic. Zinc supplementation is purported to have some efficacy in managing hyperactivity symptoms in non autistic samples, and could therefore play a role in the management of hyperactivity in autism, which is notoriously difficult.

Objectives: 1) To evaluate if young children recently diagnosed with autism or any other PDD have lower zinc levels compared to pediatric controls; and 2) to identify, within the autism sample, potential clinical correlates of zinc levels.

Methods: The study was organized in the Autism Disorder Program of the McGill University Montreal Children's Hospital; 70 children with PDD were recruited near the time of initial diagnosis and matched on age and sex to 76 pediatric controls who were all negative on an autism screening questionnaire. PDD children were evaluated with the ADI-R, the ADOS, an expert clinical evaluation, the Vineland Adaptive Behavior scales, and the Aberrant Behavior Checklist. For both groups, blood and hair samples were obtained and analyzed for zinc content using inductively coupled plasma mass spectrometry (ICP-MS) in a state-of-the art toxicology laboratory of Quebec.

Results: Cases and controls were similar with respect to age (50.3 vs 47.9 months;NS), sex (% male 88.6 vs 80.3; NS), and familial socio-demographic characteristics (family income, mother's education and ethnicity, number of siblings and birth rank, and marital status). No statistical difference between cases and controls was found for zinc levels in the blood (187.4 vs 183.3 µmol/L; NS) and in the hair (137.1 vs 143.2 µg/g; NS). Within the PDD group, parametric and non-parametric correlations between blood and hair levels of zinc were all not significant for the Social, Non-verbal communication, Repetitive behaviour scores of the ADI-R (range for r's: -0.11-0.04; all NS), for the Communication, Social Interaction and total scores of the ADOS-G (range for r's: -0.16-0.07; all NS), and for the 5 standardized scores of the Vineland scales (Communication, Socialization, Daily Living Skills, Motor skills, and ABC composite) (range for r's: -0.17-0.22; all NS). For the 51 PDD children with an ABC available, no significant correlation was found between the ABC Hyperactivity subscale and zinc blood (r=-.12; NS) and hair (r=-.14; NS) levels. Correlations for the 4 other ABC subscales and the total ABC score were equally non significant. Conclusions: There is no evidence that zinc levels are lower in young children recently diagnosed with PDD compared to pediatric controls, nor that zinc levels predict levels of functioning or autistic symptomatology in children with PDD. Furthermore, there is no evidence that hyperactivity symptoms in young children with PDD are correlated with zinc levels. Zinc supplementation is therefore not recommended as part of the routine medical management of autism.

112.39 39 Healthcare Utilization and Delay of Children with Learning and Behavioral Developmental Disabilities, National Health Interview Survey (NHIS), 2006-2007. V. G. Jarquin*[1], L. Schieve[2], K. Van Naarden Braun[3], C. E. Rice[2], S. Boulet[2] and S. Visser[2], (1)*CDC*, (2)*National Center on Birth Defects and Developmental Disabilities*, (3)*Centers for Disease Control and Prevention*

Background:

Studies document significant health impacts of many developmental disabilities (DDs). Further study of access to care is needed by disability type and race-ethnicity. We examined population-based data using 2006-2007 NHIS on healthcare utilization and delay among 15,639 children ages 3-17 with and without disabilities.

Objectives:

This study provides nationally representative estimates of health utilization and delay among US children with DDs.

Methods:

Children in three groups, autism or mental retardation (MR; N=207); attention-deficit hyperactivity disorder (ADHD) without autism or MR (N=1013); and learning disability (LD) or other developmental delay without ADHD, autism, or MR (N=720), were compared to children without DDs on healthcare indicators (e.g. seeing a medical specialist). Further analyses were conducted on 3 subgroups of children with autism/MR: autism only (N=91), MR only (N=87), and both conditions (N=24). Non-Hispanic White (NHW) and non-Hispanic Black (NHB) children were compared within each of the three main disability groups (but not the three autism/MR subgroups because of small sample sizes). Adjusted odds ratios (AOR) were calculated from logistic regression in SUDAAN to account for the complex sample design.

Results: Children in each DD group were significantly ($p<0.05$) more likely to have recently seen a medical specialist (21.0-69.1% depending on disability), mental health professional (12.5-59.7%), ancillary therapist (e.g. physical, speech, respiratory, occupational; 11.1-58.5%), and to have >9 annual healthcare visits (13.4-36.4%) than children without DDs. Associations remained significant after adjusting for sex and age. Strongest associations for each outcome were found for the autism/MR group. For example, they were substantially more likely to have seen an ancillary therapist (AOR= 37.3, 95% CI=26.2-53.0) and have >9 office visits in the past year (AOR=15.4, 95% CI=10.2-23.3). Associations for all outcomes remained extremely strong in the autism/MR subgroups. For example, the odds of recent visit(s) to an ancillary therapist were highly elevated among children with autism only (AOR=35.7, 95% CI=22.6-56.5), MR only (AOR=33.1, 95% CI=17.7-61.6), and both conditions (AOR=68.9, 95% CI=24.6-192.5). Likewise, the odds of >9 office visits in the past year were high in children with autism only (AOR=8.3, 95% CI=4.9-14.4), MR only (AOR=14.4, 95% CI=7.1-25.1), and both (AOR=7.8, 95% CI=3.4-18.1). Delayed care was associated with ADHD (AOR= 2.3, 95% CI= 1.8-3.0) and autism/MR (AOR= 3.3, 95% CI= 1.9-5.7). Associations with delayed care were also observed in children with autism only (AOR= 3.6, 95% CI= 1.8-6.6), MR only (AOR= 8.0, 95% CI= 1.1-8.1), and both (AOR= 11.6, 95% CI= 1.2-13.7). Family inability to afford prescriptions was associated with ADHD (AOR= 3.0, 95% CI= 2.1-4.1) and LD/other delay (AOR= 2.7, 95% CI= 1.7-4.1). Among children with and without DDs, NHB children had lower healthcare utilization than NHW children. However, some estimates among children with individual disabilities were imprecise, and confidence limits included 1.0.

Conclusions:

Children with DDs showed greater use of healthcare and higher prevalence of delayed care. Children with autism or MR had the highest healthcare utilization, 6-37 times higher than children without disabilities, and 2-10 times higher than children with LD/other delay and ADHD. These data inform healthcare planning for this important population subset.

112.40 40 Social Skills Training for Children with Autism Spectrum Disorders: Decreased Benefits for Children Prescribed Stimulant Medication. F. Frankel[1], E. Laugeson*[1] and B. King[2], (1)*UCLA Semel Institute for Neuroscience & Human Behavior*, (2)*University of Washington and Children's Hospital and Regional Medical Center*

Background: Social skills interventions are very important in the treatment of children with Autism Spectrum Disorders (ASD). A substantial proportion of these children have been prescribed various psychotropic medications. In our previous study of 24 children with ASD, we found that children prescribed psychotropic medication did not benefit as much from social skills training as unmedicated children. The larger number of subjects in this study will afford a finer analysis by medication class.

Objectives: This study is intended to test if children with ASD prescribed different classes of

psychotropic medication (stimulants, antidepressants, neuroleptics or no medication) by community practitioners have differential outcome after a manualized evidence-based social skills training program.

Methods: Seventy-eight 6 to 12 year-old children with Autism spectrum disorders, who were high functioning, were given 12 weeks of parent-assisted children's friendship training (CFT). Subjects were prescribed one of the following classes of medication by physicians in the community prior to treatment: antidepressants (n = 6), neuroleptics (n = 4), stimulants (n = 18) while 50 were not prescribed any psychotropic medications (Unmedicated). Two parent-rated and 3 teacher-rated social measures served as outcome variables.

Results: Results revealed that subjects prescribed stimulants were least improved on one parent-rated and one teacher-rated scales of social functioning after 12 weeks of CFT. Subjects prescribed antidepressants showed greater improvement, subjects in the Unmedicated group were next higher and subjects prescribed neuroleptics showed the greatest improvement on these two measures.

Conclusions: The present results suggest that the detrimental effects of psychotropic medication upon outcome of social skills training found in our previous research was confined to stimulants. It is not clear if the medication itself has some moderating effect on outcome, versus that children who require medication have greater functional limitations than those who do not. It is left to further research to resolve this issue.

112.41 41 Tone Discrimination in Adolescents Who Have Lost Their Autism Diagnosis: Low-Level Auditory Perceptual Abilities. I. M. Eigsti*, K. Tyson, E. Troyb, M. Rosenthal, M. Helt and D. Fein, *University of Connecticut*

Background: A variety of previous studies have found an unusually heightened sensitivity to low-level perceptual auditory distinctions in individuals with autism spectrum disorders (ASD). Adults with ASD were able to distinguish tones that differ by just 1% in frequency at a higher rate than controls (Bonnel, et al., 2003). These findings have suggested a bias toward elementary stimuli that do not require cortical or cortical-cortical processing; such a bias has been proposed to reflect a neuroanatomical bias towards local stimulus processing, and could be implicated in language deficits (e.g., if a child is unable to make generalizations about stimulus differences that are within a linguistic category; Minshew & Hobson, 2008). Objectives: Adolescents who had ASD prior to age 5 but currently do not meet criteria (i.e., optimal outcome, OO) appear to have resolved their earlier high-level social and communicative deficits. However, we do not know the extent to which they may still show basic, low-level perceptual processing characteristics (possibly due to neuroanatomical characteristics) that continue to reflect their history of ASD. Tone discrimination provides an excellent domain for assessing whether symptoms of ASD are tightly linked to a particular perceptual bias because there is significant individual variability, and typical individuals do not typically perform at ceiling. Methods: Adolescents with high-functioning autism (HFA; n = 9, mean age 13.5 years) were compared to IQ-matched OO adolescents (n = 17, mean age 12.7) and typically developing children (TD; n = 23, mean age 13.3). Groups did not differ in age (p = .58) or full-scale IQ (p = .71), though they differed in receptive vocabulary (p = .007). Participants completed a tone discrimination task modeled on Bonnel et al., 2003, in which they listened to 40 pairs of tones at each of 3 levels of difficulty: 3% (easy), 2% (medium), 1% (hard). Responses required only a same/different judgment, and all participants completed a training set, with feedback, to ensure task comprehension. Results: Performance in the easiest (3%) condition showed relatively high accuracy (M = 83% correct) relative to the 2% (75% correct) and 1% (68% correct) conditions, suggesting that participants understood the task and that the difficulty manipulation was effective. A repeated-measures MANOVA of response sensitivity (d-prime) by Group (HFA, OO, TD) and Condition (3%, 2%, 1%) with PPVT as a covariate indicated a significant effect of Group (p = .02), with no interaction, such that the HFA and TD groups differed significantly from each other; OO and HFA (p = .09) and OO and TD (p = .28) group differences did not reach significance. Conclusions: These data are consistent with previous work showing a strength in tone discrimination in HFA, a perceptual bias that may have contributed to the autistic symptomatology.

112.42 42 Early Development of Head Circumference in Autistic Children: Searching Clinical Subtypes. F. Muratori*, M. Telleschi, E. Santocchi, R. Tancredi, R. Igliozzi, B. Parrini, F. Apicella, A. Narzisi and S. Calderoni, *University of Pisa – Stella Maris Scientific Institute*

Background:

Since the first Kanner's description of Autistic Disorder, several researchers have analyzed and described the presence of an early abnormal development of head circumference in a subgroup of autistic patients who ranges from 14% to 34% in the different studies. This particular developmental trend suggest the presence of an underlying abnormal cerebral development during the first months of life and more recently it has been studied the correlation both to neuroimaging data and to clinical and neuropsychological phenotype and outcome of affected children.

Objectives:

To describe the timing of head circumference (HC) development during the first 18 months of life in patients with autism spectrum disorder (ASD). To identify subgroups of children on the basis of different pathways in early HC development and later clinical outcome.

Methods:

Longitudinal data of HC, body length and body weight during the first 18 months of life were obtained from the pediatric medical records of 50 children with ASD. All patients met DSM-IV-R criteria for ASD diagnosis which was confirmed by ADOS and CARS. IQ levels and adaptive functioning were determined respectively through psychometric tests and VABS.

Results:

More than two third of patients shows an abnormal significant increase in HC beginning at 3-5 months compared to normative data of healthy infants. In a small number of ASD children the abnormal brain growth starts from a reduced head size at birth reaching a HC normalization at the current evaluation. Another subgroup of ASD patients starts with non significant HC rate and reaches a brain size exceeding 50° percentile or macrocephaly during the first 18 months of life. Only a minority of patients shows a substantial stability or a decrease in the HC size during early infancy. Some differences have been found between types of longitudinal pathways of HC and clinical outcome.

Conclusions:

Our study confirms the evidence of a critical period in early HC development in children later diagnosed with ASD. This excessive increase occurs well before the typical onset of clinical behavioral symptoms, and it may serve as an early warning signal of risk for autism. Thus, it holds potential for clinical application because it is early, rapid, common across patients, and its detection is simple, noninvasive and objective. The hypotheses that the magnitude of abnormal HC development during infancy might be related to the severity of later clinical outcome is not confirmed, while a reduced HC at birth is significant related to a poorer outcome in cognitive level.

112.43 43 Electrocortical and Behavioral Outcomes of Novel Experimental Trial of Repetitive Transcranial Magnetic Stimulation in Autism. E. M. Sokhadze, A. S. El-Baz, J. M. Baruth, A. Tasman, G. Mathai, L. Sears and M. F. Casanova*, *University of Louisville*

Background: Previous studies by our group suggest that the neuropathology of autism is characterized by a disturbance of cortical modularity manifested as a "minicolumnar" abnormality. In this model a decrease in the peripheral neuropil space of affected minicolumns provides for an inhibitory deficit and a decrease in their signal to noise ratio.

Objectives: Given the geometric orientation of double bouquet cells within the peripheral neuropil space we proposed using low frequency transcranial magnetic stimulation (rTMS) as a way of selectively increasing the surround inhibition of minicolumns. TMS was applied over the dorsolateral prefrontal cortex of autistic patients in an attempt to strengthen the inhibitory surround of minicolumns in this area. Due to the connectivity of this brain region we expected the intervention to generalize throughout the brain, i.e., a diaschisis effect.

Methods: Eighteen patients (DSM-IV, ADI-R diagnosed) and fifteen age-matched controls participated in the study. Twelve participants with autism were assigned to the TMS group, whereas six patients formed a waiting-list group. Repetitive TMS was delivered at 0.5 Hz, 90 % of motor threshold, twice per week, with 150 pulses per day. We used an oddball task with target and non-target Kanizsa illusory figures, and non-Kanizsa standards at pre- and post rTMS treatment stages. Participants in the waiting-list group were tested twice within a month.

Results: Outcome measures based on event related potentials (ERP), induced gamma band (30 Hz–80 Hz) EEG activity, and behavioral measures pre- and post-TMS showed significant improvement. Autistic subjects as compared to controls had higher magnitude of ERP components of interest to non-target rather than target stimuli. Similar between group differences was typical for gamma. Autistic patients showed higher gamma density in response to non-target stimuli. In all autistic subjects the difference of gamma density for target and non-target Kanizsa figures was negative. TMS resulted in decrease of the amplitude in the frontal ERPs to non-target stimuli, but not to the target Kanizsa stimuli in TMS group. Effects of rTMS on the posterior ERP were significant for the latency of P3b, which decreased to non-targets, but not to targets. TMS affected the power of gamma in response to non-target stimuli on the ipsilateral frontal and parietal sites. The power of induced gamma to non-targets dramatically decreased, and difference between responses to the target and non-target items became less negative. Reaction time to targets did not change after rTMS, but response accuracy significantly increased. Results of the clinical evaluations showed that following rTMS patients with autism were reported to have reduced repetitive-ritualistic behavior as measured by the Repetitive Behavior Scales. This change was due to reduced obsessive-compulsive behaviors reported by caregivers. There was a trend toward reduction of hyperactivity following rTMS.

Conclusions: Selected electrocortical functional outcome measures were shown as sensitive markers of functional connectivity changes and improved excitatory/inhibitory balance after rTMS trial. The results suggest that the brains of autistic patients are often inappropriately activated and that rTMS offers a potential innovative therapeutic intervention.

112.44 44 Contributions of Parieto-Temporal Brain Activity, Medial-Frontal Brain Activity, and Vagal Control of the Heart to Social Skills in Children with Autism. A. Meyer*, J. Karst and A. V. Van Hecke, *Marquette University*

Background: Research investigating the neurological causes of autism indicates that social impairments in the disorder are a result of a disturbance in a ventromedial "social brain" circuit, including the parietal-temporal lobe, and in the frontal lobe. Issues processing social stimuli neurologically present behaviorally in a difficulty initiating social behaviors. The Polyvagal theory may also help explain social deficits in autism. It suggests that humans activate different neural circuits, depending on the environment, that are manifest by different heart-rate responses. If the environment is perceived as safe, the vagus nerve slows heart rate, allowing social behaviors. However, children with autism may not adequately assess risk associated with social situations, including interacting with unfamiliar people. Objectives: This poster intends to explore the neurological concomitants of social behavior in autism, as well as the role heart rate plays in children with autism's interactions with unfamiliar people. Methods: Eighteen children with high-functioning autism, ages 8-12 (mean age 10.06; 17 males), viewed a 5-minute video of an unfamiliar person reading a story. Thirteen children without autism (mean age 9.92; 10 males) were tested as a comparison group. Brain activity in the frontal and parietal-temporal lobes was measured utilizing an EEG. A 64-channel electrode cap collected data, which was analyzed using the Scan 4.3 program. Heart rate was artifact-corrected and analyzed offline. Respiratory Sinus Arrhythmia (RSA: an index of vagal control of the heart) was calculated as the variability of heart rate associated with the .12-1.0 Hz frequency band. The Social Skills Rating System (SSRS) was completed by children's caregivers to measure social skills. The data was entered into a standard, step-wise multiple regression. Results: Results indicate that the overall model was significant, $F(4, 26) = 11.07$, $p < .001$; Adjusted R squared = .573. Also, it was found that higher levels of parietal-temporal lobe activity indicated more behaviors related to autism, $\beta = .43$, $t = 2.10$, $p < .05$, while less activity in the frontal lobe suggested more behaviors associated with autism, $\beta = -.51$, $t = -2.42$, $p < .05$. More control of heart-rate (via higher RSA) indicated less behaviors related to autism, $\beta = 0.30$, $t = 2.24$, $p < .05$. Conclusions: The findings offer implications for the differences in how children with autism utilize different areas of their brains when interacting with unfamiliar people. Higher ratings of social skills were associated with a decrease in parietal-temporal lobe activity, an increase in frontal lobe activity, and an increase in vagal control of heart rate. The parietal-temporal lobe finding may be contrary to previous research, as this area is theorized to support social behavior. However, it was also found that more activity in the frontal lobe—

generally linked to executive functioning and initiating— was associated with better social skills. Lastly, it may be that children with autism exhibit less control over their heart-rate when interacting with unfamiliar people, perhaps reflecting a stress response, which affects their social behavior.

112.45 45 The Assessment of and Differences among Intellectually Disabled Adults with Comorbid Autism Spectrum Disorders and Epilepsy. K. R. Smith* and J. L. Matson, *Louisiana State University*

Background: Adults with intellectual disabilities (ID) often have comorbid Autism Spectrum Disorders (ASD) and neurological conditions such as epilepsy. Previous studies indicating of this comorbidity tend to stop short of addressing these disorders' impact on the full range of psychosocial issues, particularly in adult samples. Although psychopathology, behavior problems, and impaired social behaviors are common among those who live in institutional settings; identifying differences among adults with a single disorder or concomitant disorders has not been explored.

Objectives: The goal of this study was to systematically examine the interactions of ID, ASD, and epilepsy in an adult population through a detailed exploration of the characteristics which these disorders present in the areas of psychopathology, behavior problems, and impaired social behavior. Assessments of psychopathology, behavior problems, and social behavior were made with the ASD-Comorbidity-Adult Version and ASD-Behavior Problems-Adult Version batteries and the Matson Evaluation of Social Skills for Individuals with Severe Retardation.

Methods: Participants were residents at two state-run facilities located in the Southeastern region of the. An on-site licensed psychologist diagnosed all ID participants using DSM-IV-TR criteria (APA, 2000). Selection of participants with and without ASD in this study was based on DSM-IV-TR and ICD-10 diagnostic criteria for Autistic Disorder and PDDNOS. Inter-rater agreement within a multidisciplinary team was required in order for a classification of ASD to be made. Diagnosis of epilepsy was made by a licensed neurologist who determined classification of seizure type based on the ILAE criteria, clinical presentation, and available medical information. Ninety-two participants with ID were matched and compared across four groups, ID (n=23), epilepsy (n=23), ASD (n=23), and combined ASD and epilepsy (n=23). Participants' ages ranged from 27-78 years (mean=47.75 years, SD= 11.02 years). There were 56 males and 36 females with moderate (n=2), profound (n=88), and unspecified (n=2) ID.

Results: When controlling for age, gender, race, and level of ID, no significant differences were found across groups on measures of psychopathology. However, significant differences were found across groups on measures of behavior problems ($p<.02$) and social skills ($p<.001$). The ASD group was significantly more likely to exhibit stereotypy than the epilepsy ($p<.004$) and ID ($p<.002$) group. On measures of social behavior, the ID ($p<.02$) and epilepsy ($p<.04$) group had significantly more positive verbal behavior than the combined ASD and epilepsy group. The ID ($p<.001$) and epilepsy ($p<.001$) group had significantly more constructive nonverbal behavior than the combined ASD and epilepsy group. Lastly, the ID group had significantly more positive general aspects of behavior than the ASD ($p<.01$) and combined ASD and epilepsy ($p<.001$) group.

Conclusions: These data suggest that there are critical significant differences among ID participants expressing ID alone or ID and epilepsy from those with comorbid ASD. Specifically, individuals with ASD and combined ASD and epilepsy differ significantly on scales of stereotypy and pro-social behavior. Implications of these findings elucidate the nature and impact of these disorders.

112.46 46 EEG Theta Oscillations in Children with Autism. M. Murias*[1], S. Faja[1] and G. Dawson[2], (1)*University of Washington*, (2)*Autism Speaks, UNC Chapel Hill*

Background: Previous work (Orekhova et al., 2006) has demonstrated narrow band electroencephalographic (EEG) theta rhythms in children are reactive to attentive states, including social engagement.

Objectives: We tested whether young, high-functioning children with ASD differ in theta band EEG response during viewing of videos that contained different degrees of social content, compared with age and IQ-matched controls.

Methods: 128 channel EEG was continuously recorded as participants watched short (45 second) videos. Subjects were 21 6 and 7-year-olds with ASD and 21 age and IQ-matched controls. Diagnosis was confirmed with the ADOS,

ADI-R and DSM-IV-TR. All children in both groups had cognitive ability in the average to above average range (measured by the Differential Ability Scales). Participants sat quietly watching three short videos: (1) story telling in a foreign language (2) story telling in native (English) language; (3) comparable visual and auditory noise.
Results: Spectral analysis revealed distinct theta rhythms in most subjects in the 6-7 Hz range, with a widely distributed topography that was maximal in parietal, temporal, and frontal areas. ASD and typical children did not differ in peak theta frequency. The typical group had more pronounced theta rhythms peaks. Theta amplitudes tended to be lower in the ASD group, particularly among frontal electrodes.
Conclusions: Children with ASD appear to show altered theta range EEG reactivity during viewing of social videos. Further research is needed to determine if these amplitude reductions observed in ASD are distinct from reductions observed in alpha and mu oscillations.

112.47 47 Clinical Profile of Clients in a Specialized Dual Diagnosis Program: Comparison of Individuals with and without ASD. S. E. White*, Y. Lunsky, A. M. Palucka and M. Reid, *Centre for Addiction and Mental Health*

Background: The term "dual diagnosis" is commonly used to describe individuals with an intellectual or developmental disability (including Autism Spectrum Disorder [ASD]) and a psychiatric diagnosis. Studies have found elevated levels of psychopathology in individuals with ASD when compared to individuals with intellectual disabilities who do not have ASD. Persons with ASD have been found to be more likely to have comorbid psychiatric diagnoses, more problem behaviours, and increased use of psychotropic medications (Morgan, Roy & Chance, 2003; Bradley & Bolton, 2006; Bradley, Summers, Wood & Bryson, 2004; Brereton, Tonge & Einfeld, 2006; Tsakanikos et al., 2007). These findings, however, are not universal (i.e., Tsakanikos et al., 2006), and may not hold true for individuals in our clinical (as opposed to community) sample, the majority of whom come in to the program with an existing psychiatric diagnosis. Nevertheless, it may be that individuals with ASD in specialized "dual diagnosis" programs present with more severe psychopathology and more behavioural challenges than individuals with an intellectual disability only. Palucka and Lunsky (2007) and Prichard et al. (2007) have described characteristics of clients with ASD in a tertiary level "dual diagnosis" program. However, a more detailed comparison of the diagnostic and behavioural profiles of dually diagnosed clients with and without ASD has not been conducted.
Objectives: The present study sought to expand upon the findings of previous research by comparing the clinical profiles of clients with and without ASD referred to a "dual diagnosis" psychiatry service for individuals with intellectual disabilities. In particular, we analyzed differences in demographics, psychopathology, medication use, and behavioural symptomatology, as assessed using the Aberrant Behaviour Checklist (ABC) and Reiss Screen for Maladaptive Behaviour.
Methods: We reviewed the charts of a subset of clients (n = 74) who received services from a specialized "dual diagnosis" program from 2006 to 2008. The sample was subdivided into an ASD (n = 21) and a non-ASD (n = 53) group, based on the diagnosis at the time of admission. For all clients, the ABC and Reiss were completed by caregivers within one month of beginning service.
Results: Demographically, there were more men in the ASD group (χ^2 (1,74) = 8.90, $p < 0.01$), with no other differences terms of ethnicity, age, or residential setting. Clinically, clients with and without ASD did not differ in their psychotropic mediation use, or Reiss and ABC scores, with the exception of higher scores for the ASD group on the autism (t(71) = 2.28, $p < 0.05$) and psychosis (t(71)=2.19, $p < 0.05$) subscales of the Reiss. Diagnostically, there was a trend towards lower rates of mood disorders in the ASD group (χ^2 (1,74) = 3.32, p = 0.07).
Conclusions: Contrary to the findings of previous research, individuals with ASD in this clinical sample exhibited the same range of psychopathology and maladaptive behaviour as other individuals, according to caregiver ratings. Future research with a larger client sample is needed to further refine the psychiatric profile of individuals with ASD. Interpretation and implications of the findings are discussed.

112.48 48 The Development of Perceptual Expertise for Faces and Objects in Autism Spectrum Conditions. C. Damiano*[1], O. Churches[2], H. Ring[2] and S. Baron-Cohen[2], (1)*Vanderbilt University*, (2)*University of Cambridge*

Background: The high perceptual demands of human social interaction necessitate expertise for the rapid processing of faces. However, previous research indicates that this expertise for faces may be impaired in individuals with autism spectrum conditions (ASC). It is unclear if this

deficit is related to a lack of social motivation or to a more general cognitive impairment associated with the process of gaining expertise. Furthermore, there is very little empirical evidence describing how individuals with ASC acquire perceptual expertise or how this process compares to expertise development in typical individuals.

Objectives: (1)To determine if face processing deficits in ASC are attributable to a lack of experience-dependent expertise with faces or to a more general deficit in gaining expertise. (2) To examine the extent to which individuals with ASC can develop expertise with a set of novel objects. (3) To compare the perceptual strategies developed for expertise processing to those involved in face processing, to determine if these mechanisms are functionally independent in individuals with and without ASC.

Methods: This experiment was comprised of three parts: an initial session in the laboratory, ten sessions of expertise training, and a second laboratory session following training. In the laboratory sessions, participants performed two tasks: an inversion effect task and a composite effect task. As a measure of performance, response time and accuracy data were collected for both tasks. Between laboratory sessions, participants completed ten sessions of a training program with a set of complex, novel objects, known as *Greebles*. Like faces, *Greebles* can be categorized on basic and subordinate levels according to configural relationships among parts. Expertise was empirically defined as automatic subordinate level processing of *Greebles*.

Results: Individuals with ASC successfully developed perceptual expertise with *Greebles*, requiring the same quantity of experience to reach expertise as typical individuals. As experts, individuals with ASC showed a *Greeble* composite effect, but failed to show a significant *Greeble* inversion effect. Typical individuals, on the other hand, showed both composite and inversion effects. Furthermore, while typical individuals showed improvement specific to upright faces, individuals with ASC showed significant improvement on both upright *and* inverted faces.

Conclusions: The face processing deficit in ASC is likely to be attributable to a face-specific deficit in holistic processing (indexed by the composite effect), along with a more pervasive deficit in configural processing (indexed by the inversion effect). Therefore, both social and more general cognitive or perceptual models can be used to explain this impairment. Because *Greeble* training had an effect on face processing, these results suggest that at least some of the same neural substrates underlie face and expertise processing, providing further support for the expertise hypothesis. These findings indicate that with sufficient motivation and training, individuals with ASC show significant gains in expertise processing. However, these gains may be limited by general perceptual impairments that cannot be ameliorated even with extensive experience. Future face processing interventions should focus on encouraging greater social interest and on enhancing compensatory strategies to take into account the perceptual deficit in ASC.

112.50 50 Using Semantic Web Technologies to Standardize a Catalog of Autism Phenotypes. A. K. Das*, L. Tennakoon and S. W. Tu, *Stanford University*

Background: The multiple ways that autism investigators define clinical phenotypes can lead to challenges in understanding what research findings are being established, communicated, and shared.

Objectives: As part of the development of the National Database of Autism Research (NDAR) (http://ndar.nih.gov/), which will maintain and share data gathered by standardized clinical assessments in NIH studies, we are developing an ontology, or formal knowledge model, to standardize and catalog the definitions of phenotypes. The resulting ontology will allow NDAR users to query high-level concepts, such as age of first spoken word, without needing to understand the low-level representation of how such data is stored.

Methods: To define the scope and content of the ontology, we first undertook a requirements analysis to gather the range of concepts, relationships, and abstractions used in autism research. We undertook a literature search of the PubMed database used the key words "(ADI R or ADOS or Vineland) and (genes or genetics) and autism." We then created a list of those phenotype definitions that were used as eligibility criteria or analytic studies in an original research study. We identified a unique set of definitions, and then determined whether the phenotype definition could be encoded using the Semantic Web ontology and rule language standards, OWL and SWRL, respectively.

Results: We found 43 published research papers as of March 1, 2008, and selected 26 of these as relevant based on the inclusion criteria of studies who enrolled subjects with a diagnosis of autism and were published in the English language. Excluding criteria used for diagnosis of autism or autism spectrum disorder, we found 75 uniquely defined concepts used as candidate phenotypes (mean of 4 concepts per paper). Nearly two-thirds of the concepts (63%) were based on a one-to-one mapping with a single item on an assessment instrument, sometimes using a cutoff score. Approximately one quarter (24%) were defined as abstractions that were the sum of several items, where such a score was not already an instrument item. The remaining concepts (13%) were not defined clearly enough by the authors to be mapped precisely to a discrete set of items. Among this set of concepts, several were used for analysis across multiple papers. Some concepts were slight variations of each other; for example, different cutoff scores used to define presence or absence of a savant-skill phenotype. Of the 65 phenotype descriptions that we could map precisely to instrument items, we were able to encode all of them using the OWL and SWRL formalisms.

Conclusions: The results of our analysis of phenotype concepts in the autism research literature indicate the need for a well-defined set of clinical phenotypes. The ontology-based framework that we are developing for NDAR can provide a common, standardized core set of concepts and relationships to unify diverse clinical, behavioral, and genetic data on autism; allow investigators to share, query and integrate stored data using common terms; and serve as a computational catalog that tracks the evolution of candidate phenotypes.

112.51 51 The Clinical Validity of Childhood Disintegrative Disorder.

A. Westphal*[1], K. Koenig[1] and F. R. Volkmar[2], (1)*Yale Child Study Center*, (2)*Yale University School of Medicine*

Background: "Childhood Disintegrative Disorder" (CDD) is a rare ASD in which typically developing children over two years old undergo a severe and mostly irreversible regression of developmental gains. Like the other ASDs, CDD is characterized by social and language disabilities, as well as rigid and repetitive patterns of behavior, and is estimated to occur in 1-2 children per 100,000. With the categorization of CDD as an entity distinct from other ASDs, it became important to determine whether CDD cases were merely examples of late onset "regressive" AD. Volkmar and Cohen have compared a group of children with CDD diagnoses to a group of children with autism that had been recognized after two years of age, and found that the children with CDD had accumulated more skills prior to regression, and ultimately had significantly greater impairment in speech and intellectual disabilities than children with regressive autism. They concluded that the 'clinical features at the time of regression and various outcome measures support the validity of the diagnostic concept, particularly when such cases are compared to "late onset" autistic ones.'

Objectives: The objective of this study is to compare these groups in terms of long-term outcomes with the intention of gathering further information on whether there is any prognostic validity to the distinction between CDD and other ASDs. Previous studies have examined level of function immediately subsequent to regression, and found that children with CDD fare much worse in multiple domains. However it is not clear that these differences are sustained over longer periods. A secondary purpose is to further characterize this rarely studied disorder in a sample of children larger than any previously described.

Methods: We compare two groups of children, one with CDD and one with Autistic Disorder (AD) using, at baseline, a series of measures including the ABC, ADOS, and CARS and the Vineland. We follow up with this group on average 8 years subsequent to the initial visit to determine outcome in terms of social, cognitive, linguistic and behavioral function.

Results: Preliminary trends corroborate previous findings: 1) Children with CDD experience deterioration across multiple domains, particularly noticeable in the decay of self-help skills, whereas in AD, regression is often isolated to language. 2) The onset of CDD is rapid, whereas with regressive AD is insidious. 3) Children with CDD more frequently have seizure disorders. 4) Children with CDD have higher levels of anxiety and stereotypies. Data on the long-term outcomes of the group with CDD is still being collected.

Conclusions: In that these variables are not diagnostic criteria for CDD, but distinguish CDD from regressive AD, they support the clinical validity of the disorder. The presence of both

CDD-like regressions among children falling into the AD category and of subtle, early developmental delay among some CDD cases could be taken as evidence of continuity between CDD and AD. On the other hand, this evidence could also support the diagnostic concept of CDD, marking the presence of a distinct and recognizable clinical entity which occasionally defies its' diagnostic tethers.

112.52 52 Advancing Early Detection of Autism Spectrum Disorder by Applying An Integrated Two-Stage Screening Approach. R. J. Van der Gaag*[1], I. J. Oosterling[2], M. Wensing[1], S. Swinkels[3], J. K. Buitelaar[4], R. B. Minderaa[5] and M. P. Steenhuis[6], (1)*Centre for Quality of Care Research, Radboud University Nijmegen Medical Centre, The Netherlands*, (2)*Karakter University Centre*, (3)*Karakter Child and Adolescent Psychiatry University Center*, (4)*Radboud University Nijmegen Medical Centre, Nijmegen Centre for Evidence-Based Practice*, (5)*University Medical Center Groningen*, (6)*University of Groningen and University Medical Center Groningen*

Background:

Few field trials exist on the impact of implementing guidelines for the early detection of Autism Spectrum Disorders (ASD).

Objectives:

The aims of the present study were to develop and evaluate a clinically relevant integrated early detection programme based on the two-stage screening approach of Filipek et al. (1999), and to expand the evidence base for this approach.

Methods:

The integrated early detection programme encompassed training relevant professionals to recognize early signs of autism and to use the Early Screening of Autistic Traits Questionnaire (Swinkels et al., 2006; Dietz et al., 2006), use of a specially developed specific referral protocol, and formation of a multidisciplinary diagnostic team. The programme was evaluated in a controlled study involving children in two regions: experimental versus control region (N=2793, range 0-11 years). The main outcome variables were a difference in mean age at ASD diagnosis and a difference in the proportion of children diagnosed before 36 months.

Results:

ASD was diagnosed 21 months (95% CI 9.6, 32.4) earlier in the experimental region than in the control region during the follow-up period, with the mean age at ASD diagnosis decreasing by 19.5 months (95%-CI 10.5, 28.5) from baseline in the experimental region. Children from the experimental region were 9.4 times (95%-CI 2.1, 41.3) more likely than children from the control region to be diagnosed before age 36 months after correction for baseline measurements. Most of these early diagnosed children had narrowly defined autism with mental retardation.

Conclusions: This programme for the early detection of ASD appears to be clinically relevant and led to the earlier detection of children with ASD, mainly in combination with low IQ.

112.53 53 Autism Symptom Clustering Scale: a Tool for Management of ASD. M. Brimacombe* and X. Ming, *New Jersey Medical School - UMDNJ*

Background: Autism spectrum disorder (ASD) is a neuro-developmental disorder defined across a wide spectrum of diagnostic elements. This complicates attempts to develop an overall measure or index of management burden.

Objectives: Here the focus is on identifying a useful set of clinically relevant symptoms to develop an Autism Symptom Clustering Scale (ASCS) relevant to the assessment of caregiver burden.

Methods: Using a case cohort of 160 autistic patients, an ASCS score based on weighted averages of symptom dimensions defined clinically and via principal components is developed for Asperger's, PDD-NOS and clinical autism groups that together make up the autism spectrum.

Results: The ASCS score differentiates the clinical autism group versus other sub-groups making up the autism spectrum. The burden measure is also examined across gender and age group demographic sub-groups.

Conclusions: This work demonstrates that it is possible to develop useful clinical symptom based scales relevant to the identification of case management related sub-groups within the ASD diagnostic spectrum.

112.54 54 Development and Validation of the Autistic Learning Disabilities Inventory (ALD-I): Operationalizing Autistic Symptomatology for Individualizing Treatment. B. Siegel*[1], A.

Bernard[1], C. Cerros[2], W. Mu[3] and T. Sendowski[1], (1)*University of California, San Francisco*, (2)*University of Washington*, (3)*Wellesley College*

Background:
Significant work has focused on valid and reliable identification of autistic spectrum disorders (ASDs), as well as its evidence-based treatment. However, there remains a gap in moving systematically from signs of ASDs to individualized selection of treatments based on these clinical characteristics. We report on development of the ALD-I, a measure designed to operationalize autistic symptomatology so treatments can be selected that target a S's specific key deficits. To accomplish this, ASDs were reconceptualized as a constellation of autism-specific learning disabilities (ALD) and autism-specific learning styles (ALS) that can then be mapped onto treatments that target deficits in key domains. Doing this can facilitate outcome research where groups can be matched or co-varied according to ALD-I profile, or outcome can be examined with respect to specific ALD.

Objectives:
We will present factor analytic data supporting the validity of the ALD-I for identification of key domains of ASDs. Cohesive clinical sub-domains on each factor will be described with respect to independence, internal consistency, and variance accounted. Procedures in instrument development (e.g., item inclusion, deletion and scaling) will be reported.

Methods:
The Autistic Learning Disabilities Inventory (ALD-I) (N=164) was completed by primary caregivers of Ss age 4 – 17 years referred for ASD evaluation. The initial ALD-I was formulated as a 68-item questionnaire using a 5-point Likert Scale. The items were theoretically clustered into 3 domains: Social, Communication and World of Objects. Within each domain 3-4 sub-domains scaled the items into specific skill areas (e.g., Imitation). For item selection/ retention analyses, Ss were grouped into two diagnostic categories: Autism (AD) and ASD (Autism, Asperger's, and PDD-NOS). Comparative data were also collected on ASD-referred Ss later found to meet criteria for mental retardation, ADHD or a language disorder. A further 225 comparable cases received ALD-Is with simplified 3-point scaling analyzed later.

Results:
The goals of data analysis were to 1) derive factors to identify empirical ALD and ALS domains and sub-domains, 2) describe internal consistency of sub-domains, 3) calculate differential (mean, standard deviation) scores on these factors and sub-domains in study and comparison groups, and 4) eliminate redundant, unreliable and non-loaded items. Initial rotated factor analysis of 5 point data identified 3 distinct factors with factor loadings ≥ .35- I: 'World of Objects,' II: 'Social and Non-Verbal Communication' and III: 'Verbal' (with respective variance accounted= 7.5, 7.2, and 4.9). A comparison of factor score sums across diagnostic groups revealed significant differences between AD, ASD and comparisons, as did parallel analyses of sub-domains for each factor.

Conclusions:
The ALD-I measures a coherent set of social, verbal and play skills useful in identifying specific learning deficiencies as well as relative strengths for ASD children. The measure should be useful in 1) identifying Ss with deficits likely to respond to specific treatments, 2) identifying relative strengths that can be capitalized upon for treatment, and 3) designing treatment research where explication of characteristics of responders is valuable.

112.55 55 CARS and ADI-R Profiles of Children with Asperger Syndrome in Comparison with Those with Autism. J. H. Schroeder*[1], J. Bebko[2], J. A. Weiss[3], K. McFee[1], C. A. McMorris[1], L. Hancock[2] and K. Wells[2], (1)*York University, Toronto*, (2)*York University*, (3)*Centre for Addiction and Mental Health & York University*

Background: Researchers and clinicians use a variety of diagnostic measures both in identifying the presence of and further determining the severity of autism and Asperger Syndrome (AS). This variability has led several researchers to question the validity of the Asperger Syndrome diagnosis. Thus, further research would be beneficial for determining the fundamental characteristics of these conditions.

Objectives: To compare the Childhood Autism Rating Scale (CARS) and the Autism Diagnostic Interview-Revised (ADI-R) profiles in a sample of children with AS relative to a sample of children with Autism.

Methods: Eighteen children with AS will be compared with twenty children with Autism. Participants range in age from 6 to 17 years. The CARS and the ADI-R were administered to determine Autism symptom severity. Intellectual abilities (assessed using the Wechsler Abbreviated Scales of Intelligence), receptive (measured using

the Peabody Picture Vocabulary Task) and expressive language (measured using the Expressive One-Word Picture Vocabulary Task) levels were assessed.

Results: Preliminary results indicate that mean Autism severity scores on both the CARS and the ADI-R are lower in the AS group than in the Autism group. The frequency of endorsement for particular CARS and ADI-R items between groups will be discussed, and the predictive power of each item and of language and intelligence scores will be reported.

Conclusions: This study will help to determine the validity of using the CARS and the ADI-R with individuals with AS. In addition, this research will further our understanding of the characteristics of Asperger Syndrome, and also the validity of the Asperger Syndrome diagnosis.

112.56 56 IMFAR Analysis in Support of NDAR Strategic Requirements. D. Hall*[1], J. Chung[2] and G. Navidi[1], (1)*National Institute of Mental Health, National Institutes of Health*, (2)*Georgetown University Medical School*

Background: The National Database for Autism Research (NDAR) is a collaborative biomedical informatics system sponsored by the National Institutes of Health. Primary objectives of NDAR are to provide broad access to high quality, detailed human subjects data that underlie research findings relevant to autism spectrum disorders (ASD) and to facilitate data sharing. Sharing of phenotypic, genetic and imaging data provides the opportunity for researchers to (a) validate research results, (b) pool standardized information, (c) use data collected by others to explore hypotheses not considered by the original investigator. NDAR also uses a global unique identifier (GUID) that allows researchers to identify data from a particular subject across multiple studies using a secure method.

Objectives:

To characterize the type of research data and typical sample sizes of recent ASD research studies using information available from abstracts of the 2008 International Meeting for Autism Research (IMFAR). This analysis was carried out to better understand how NDAR can contribute to advancing and accelerating ASD research.

Methods:

The 779 poster and oral presentation research abstracts were reviewed for the following information:

· Abstract topic - by IMFAR category

· Whether the research included human subjects or biomaterials

· Sample size of enrolled human subjects with ASD as well as controls

· Specific clinical assessments/measures disclosed

· Whether the study focused on NDAR relevant categories of neuroimaging, genetics, treatment/intervention, or phenotyping

A priori exclusion criteria were established to confine subsequent analyses to studies most appropriate for inclusion in NDAR. The exclusion criteria were:

· The study did not involve human subjects or the number of human subjects was not reported (123 studies)

· The research focused on the development or validation of measures/assessments (40)

· The study involved cell/animal models (25)

· The research involved a literature review, bioinformatics system review, or survey of treatment providers (19)

· The study reported on a large self-selected survey population or online questionnaire (19)

· The study was an epidemiology study (38)

Results:

Of the 779 abstracts, 510 (65%) involved human subjects or human biomaterials. The average sample size of IMFAR studies involving human subjects is 67 with a standard deviation of 118. The median sample size is 24.

Analysis of sample sizes for specific types of studies: Mean (SD)

Treatment/Intervention (70 studies) – 31 (73)

Phenotyping (323 studies) – 60 (99)

Genetics (47 studies) - 218 (219)

Neuroimaging (57 studies) – 21 (15)

Conclusions:

This analysis provides evidence that relatively small sample sizes are the norm in ASD research and that a large portion of autism studies focuses on phenotype data. The mean sample sizes differ by study type with genetics studies having larger sample sizes than imaging studies. Of particular note are the small samples sizes for treatment/intervention studies, which generally require larger numbers of participants to have sufficient power to demonstrate efficacy. It is our belief that community adoption and support of a bioinformatics platform such as NDAR could help increase scientific collaboration/corroboration, thereby increasing study power, and data sharing, and other efficiencies.

112.57 57 Development of a Functional Classification System for Children with Autism Spectrum Disorder: Starting the Process. B. M. Di Rezze*[1], V. Thakur[1], P. Rosenbaum[1] and L. Zwaigenbaum[2], (1)*McMaster University*, (2)*University of Alberta*

Background: Despite the availability of measures to assess the symptoms of children with autism spectrum disorder (ASD), none has reliably and validly described ASD along a spectrum of functional ability. Clinical diagnostic tools such as the Autism Diagnostic Observation Schedule, the Child Autism Rating Scale and the Autism Diagnostic Interview- Revised aim to discriminate children with ASD from children with other disabilities. Furthermore, ASD classification has also focused on identifying multi-dimensional phenotypes that are potentially relevant to describe symptom severity. One area that has not been examined is how a diagnosis of autism translates in terms of a child's functional abilities. This focus of classifying functional ability has been prevalent in the study of cerebral palsy (CP) since the late 1990's. Research in CP has led to the creation of condition-specific discriminative systems to classify the levels of gross motor function (GMFCS) and manual ability (MACS), with a communicative function system currently under development. This array of functional measures aims to describe, classify, and predict function, as well as to evaluate change in status over time. An analogous system for ASD (the AFCS) would provide an internationally acceptable method of stratifying function in children and improving communication with families and professionals about abilities and needs.

Objectives: To develop a survey for experts working with pre-school children with ASD to establish an initial draft of an Autism Function Classification System (AFCS).Methods: The process of creating the initial draft of the AFCS included a scoping review of the literature to assist with the development of the questions. The review involved a search of health care databases (1980-2008); consultations with expert clinicians and researchers; and a review of classifications used in clinical practice. The principles of survey development were based on the Dillman method, and surveys will be completed online.

Results: The survey instrument will explore the following questions (with appropriate response options): What methods do you use to diagnose ASD? Do you diagnose on a multi-disciplinary team? What are the salient functional and behavioural features of ASD that you consider with a 3-4 year old who may have the condition? How important are language abilities/cognitive function/social behaviours/ repetitive behaviours in making the diagnosis of ASD (score 1-5)? Do you assign higher weighting to specific symptoms (rank in order of importance)? Do you give consideration to functional or qualitative evaluation of ability? Do you use the terms 'high functioning' or 'low functioning' when describing a child with ASD? What are the characteristics of these subgroups?

Conclusions: It is unclear from the literature and clinical practice how functional ability is described within the current systems of ASD classification. The developed survey aims to establish the key attributes that characterize the functional severity of a child with ASD to form an initial draft of the AFCS. A select group of international expert respondents have agreed to participate in the web-survey. The interactive poster will discuss the results of the analysis of survey responses and will use the format to welcome further input based on emerging follow-up questions.

112.58 58 Description of the RESEARCH Group on Pervasive Developmental Disorders in SÃo Paulo- Brazil. R. L. Velloso, A. A. Vinic, S. H. B. Ribeiro, C. S. de Paula*, D. Brunoni and J. S. Schwartzman, *Universidade Presbiteriana Mackenzie*

Background: The Pervasive Developmental Disorders (PDD) includes a broad spectrum of disorders of development characterized by the

presence of disturbances in social skills, in communication and behavior, with restricted and repetitive interests. Diagnose correctly the PDD and conduct research in this area is very important for the knowledge of professionals who work in the area and interventions ever earlier.
Objectives: Describing the group of research and evaluation on PDD of the Post-Graduate Program of Developmental Disorders, Center for Biological Sciences and Health, Mackenzie Presbyterian University, São Paulo, Brazil.
Methods: Description of the protocol of evaluation and analysis of the database group's evaluation of PDD.
Results: The evaluation: anamnesis, screening questionnaires (SCQ: Social Screening questionnaire, ABC: Autism Behavior Checklist), neuropsychological assessment (WISC III, PEP-R, Trail Making Test, Wisconsin test, Rey) evaluation speech with an emphasis on language and social cognition (Pragmatic, Language Competences, Symbolic Maturity, Shared Attention, Empathy Card-deck, card-deck of basic facial expression in photos and drawings, Theory of Mind tasks, Social Stories Questionnaire), physical examination, neurological examination, assessment by equipment that records the eye movement (Tobii eye tracking) and implementation of protocols for scientific research. At the end of each assessment, the group concludes a diagnosis. Then it is done with a report of conduct and guidelines, which are explained in a meeting with the family of the individual assessed. From 2007 until 2008 were assessed 38 subjects, with 30 subjects were male and 8 female, aged between 2 and 39 years, with the largest concentration 5 to 11 years.
Diagnostics: 8 subjects did not meet criteria for PDD, 8 received a diagnosis of PDD, 7 of autism, 6 of Asperger Syndrome, 8 of Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS), and 1 with a semantic pragmatic disorder.

Conclusions: The group described conducts research and evaluations, reiterating the importance of the development of knowledge in the area, suitable for early intervention.

112.59 59 Detailed Information Perception in Adults with HFA or Asperger Syndrome; Assessment and Interpretation. A. A. Spek*[1], E. M. Scholte[2] and I. A. van Berckelaer-Onnes[2], (1)*Mental Health Institution Eindhoven*, (2)*Leiden University*

Background:

The weak central coherence account has been modified. A local or detail-focused information processing style seems crucial in autism. Research in detailed information processing in adults with ASD is limited; it remains undetermined if, and to what extent adults with HFA or Asperger syndrome have an enhanced local perception. Most studies used neuropsychological tests to assess detailed information processing, although no test have been developed specifically with this aim. Self-reports have not been used to measure detailed information perception in individuals with ASD. However, the 'explicit' theory of mind of adults with ASD may enable them to recognize and describe their strengths and weaknesses adequately.

Objectives:

To examine whether adults with HFA or Asperger syndrome have a detailed information processing style, results of two neuropsychological tests and two self-report questionnaires have been compared to a matched group of neurotypical individuals. Correlations between the tests and the questionnaires have been used to assess validity of the instruments. Further, the influence of processing speed on detailed information perception has been investigated.

Methods:

Forty-two (42) adults with high functioning autism, forty-one (41) adults with Asperger syndrome and forty-one (41) matched neurotypicals participated in the study. The groups were matched in age, gender, handedness, full scale IQ and verbal abilities. The ADI-R was used in the diagnostic process, differentiation between HFA and Asperger was based on criteria of ICD-10 and Gillberg & Gillberg. In the assessment of detailed information perception, the Embedded Figures Test and the Block Design subtest of WAIS III were used as neuropsychological tests and the Systemizing Quotient and the subscale 'attention to detail' of the Autism Spectrum Quotient were used as self-reports.

Results:

The three groups did not differ in performance on the Block Design task. In the Embedded Figures Task, the neurotypical group showed significantly

better performance compared to the HFA group, which can be attributed to the relatively low processing speed in the HFA group. Absent, or only weak correlations were found between self-reported detailed information processing and the two neuropsychological tasks in the three groups. The HFA and Asperger syndrome groups reported higher levels of self-perceived detailed information processing and a stronger tendency to use systemizing strategies compared to the control group.

Conclusions:

The present study indicates that adults with HFA or Asperger syndrome are, at least partly, capable of recognizing their tendency to detailed information processing. In this area, they have more self-knowledge and introspective abilities than previously thought. The results further suggest that the EFT and the Block Design task may not be valid indicators of detailed information processing in adults in general. In assessing detailed information perception in adults with HFA or Asperger, the use of self-reports might be preferred over the use of neuropsychological tasks. The present study further indicates that systemizing may be a way of coping with a detailed information perception for the two disorder groups, but also for the neurotypical group. This confirms recent theories describing detailed information processing as a cognitive style, rather than a deficit in central coherence.

112.60 60 Parent and Teacher Ratings of Executive Function Deficits Related to ADHD--Not Autistic--Symptomatology. D. A. Pearson*[1], K. A. Loveland[1], M. G. Aman[2], C. W. Santos[1], C. D. Casat[3], R. Mansour[1], S. M. Elliott[1], P. I. Factor[1] and L. A. Cleveland[1], (1)*University of Texas Medical School at Houston*, (2)*Ohio State University*, (3)*Carolina NeuroSolutions, LLC*

Background: Many children with autism have significant symptoms of ADHD (i.e., inattention, hyperactivity, impulsivity). Given that executive functioning (EF) deficits are associated with ADHD, children with autism who also have significant ADHD symptomatology may be at high risk for EF deficits. If these EF deficits exist, it is not known whether or not they would be more closely associated with the child's ADHD symptoms or with his or her autistic symptomatology.
Objectives: The purpose of this study was to examine the relationships between behavioral ratings of 1) executive functioning (EF) deficits, 2) autistic symptomatology, and 3) ADHD symptomatology in children with autism.
Methods: Participants were 56 children (42 boys; mean age=9.3 yrs; mean IQ=80) who met DSM-IV criteria for autism on the ADI-R and the ADOS. For both parents and teachers, relationships between the following measures were assessed using correlational methods: The Behavior Rating Inventory of Executive Function (BRIEF), the Social Communication Questionnaire (SCQ; autistic symptoms), and the Conners Rating Scales (ADHD symptoms).
Results: Children with autism who had more severe ADHD symptomatology were found to be at significantly higher risk for a broad spectrum of EF deficits, relative to those with milder ADHD symptomatology. In contrast, more severe levels of autistic symptoms were generally not associated with an increased risk for EF deficits. These findings were similar for parent and teacher ratings.
Conclusions:

Findings suggest that children with autism and significant ADHD symptoms—as opposed to children with autism alone—are at high risk for executive function deficits, and their associated academic and social sequelae. Given that EF deficits associated with ADHD in the general school age population are often successfully treated with stimulant medication, it may be the case that the EF deficits associated with ADHD in children with autism may also be responsive to similar treatments.

112.61 61 Validity and Reliability of a New Measure of Joint Attention in School-Age Children and Adolescents. J. L. Bean* and I. M. Eigsti, *University of Connecticut*

Background:
Joint attention, the ability to share focus with another person in relation to an object or event in the environment, is an essential developmental milestone and one of the earliest markers of Autism Spectrum Disorders (ASD). Joint attention is thought to directly influence children's language acquisition, theory of mind development, and social cognition skills. However, research is limited in regards to joint attention skills and the developmental consequences in later childhood and adolescents. We present preliminary data from a measure of joint attention skills in older children and adolescents.
Objectives:
The first goal is to support the validity of this joint attention measure through correlations with an

established measure of early social development (Social Communication Questionnaire, SCQ). The second goal is to evaluate the measure's ability to discriminate between an ASD and a typically developing (TD) group.

Methods:

The measure consists of eight naturalistic prompts, four verbal and four nonverbal, designed to elicit initiation of and response to joint attention. Children receive a score based on the characteristics of their response to each prompt. Prompts include, e.g., calling his/her name, gazing to a target behind the participant, etc. The measure was piloted with 15 15 typical adults (ages 18-21) to establish its appropriateness, interrater reliability, and psychometric stability. In addition, data were collected from (to date) eight children, ages 7 to 14 years. Four children with ASD were matched to 4 typically developing controls on chronological age, p = .68 (ASD M = 10.5, TD M = 11.3 years) and IQ, p = .85 (ASD M = 103.8, TD M = 105.3). ASD diagnosis was established with the ADOS and ADI. Final analyses will include data from 40 children (ASD n = 20) ages 6 to 16 years.

Results:

The ASD and TD groups differed significantly in total score for the joint attention measure, p = .01 (ASD M = 16.75, TD M = 24.25), indicating that the ASD group was significantly less responsive to joint attention prompts and less likely to initiate joint attention episodes. Importantly, there was individual variability within both groups, with scores ranging from 16 to 17 (ASD) and 19 to 28 (TD) from a total possible score of 32. Furthermore, the joint attention measure was significantly correlated with SCQ scores, r = -.724, p = .04.

Conclusions:

While preliminary, these exciting data suggest that joint attention continues to impact social interactions in individuals with ASD, even during late school-age and early adolescence. Drawing on a full dataset, these data will indicate whether joint attention is measurable via a straightforward, psychometrically-valid measure. Given the demonstrable consequences of atypical joint attention, such an assessment tool would be highly useful and clinically valuable.

112.62 62 Differences in Parental Reports of Behavior: a Possible Factor in Disparities of Age at Diagnosis of Autism Spectrum Disorders in African Americans. A. R. Wimsatt, A. Rozga* and D. L. Robins, *Georgia State University*

Background:

Earlier detection and subsequent implementation of intervention services yields the best outcome for children with autism spectrum disorders. Accordingly, measures are being taken to reduce the overall age at which ASDs are detected. However, recent research has found that African-Americans are diagnosed an average of 1.5 years later than Caucasian children and are more likely to receive a misdiagnosis of adjustment disorder or conduct disorder prior to their ASD diagnosis than other children (Mandell et. al., 2002, 2007).

Objectives:

This study examined the impact that varied racial and educational backgrounds may have on the diagnostic process of young children with autism. It is possible that differences in initial diagnoses may be related to differences in frequency of reports or specific nature of concerns that parents of particular racial or educational backgrounds report to health care professionals. This study tested the hypotheses that 1) African-American parents report fewer concerns corresponding to specific symptoms of ASDs and place more emphasis on disruptive behaviors than other racial groups, and 2) Parents with fewer years of formal education report fewer ASD-specific concerns and place more emphasis on disruptive behavior than more highly educated parents.

Methods:

As a part of a diagnostic evaluation, developmental history questionnaires were administered to parents of toddlers who screened as 'at risk' for autism (mean age at evaluation= 26.11 months, *SD*= 4.47 months) as a part of a larger ongoing study for the early detection of autism. Parents' (N = 300) free responses to specific open-ended items on a history questionnaire, such as 'What concerns you most about your child's development?' and 'What made you initially concerned about your child's behavior?', were compared based on race and maternal education reporting differences. Open-ended responses were classified according to whether the parent noted a behavioral characteristic specific to children with ASDs and/or if they emphasized the child's disruptive behaviors.

Results:

Analyses revealed a significant main effect of race on frequency of ASD-specific concerns, $p = .03$. Specifically, it was found that African-Americans ($M = .93$, $SD = .18$) reported significantly fewer ASD-specific concerns than Hispanic/Latinos ($M = 1.7$, $SD = .20$), $p = .05$. Results also revealed a significant main effect of race on frequency of reports emphasizing non-compliant behaviors $p = .001$. Specifically, Hispanic/Latinos reported significantly more disruptive concerns ($M = .55$, $SD = .10$) than both Caucasians ($M = .29$, $SD = .04$) and African-Americans ($M = .10$, $SD = .10$), $p < .01$. There were no significant maternal educational differences.

Conclusions:

Hypothesized differences between African-Americans and other races in terms of ASD-specific reports were only partially supported by the data; differences in age at diagnosis for African-Americans may be due to other factors such as continuity of health care. Similarly, it is possible that there is a disconnection between parental expression of concern and referral for evaluative services. Because African-Americans actually reported fewer concerns of disruption, misdiagnoses of African-Americans with conduct and adjustment disorder may not be directly related to parental misattribution of symptoms. It is possible that underlying expectations about African-American behavior in general may lead to misattribution of any observations of disruption.

112.63 63 Prediction of Outcome after One Year of Early Intensive Behavioral Intervention. T. Smith*[1], R. Klorman[1] and D. W. Mruzek[2], (1)*University of Rochester*, (2)*University of Rochester Medical Center*

Background: During early intensive behavioral intervention (EIBI), which begins prior to the age of five years and involves 20-40 hours per week of treatment, some children with autism make large developmental gains. However, outcomes vary widely across children, and reliable predictors of differential response are unavailable for this expensive treatment.

Objectives: Examine predictors of outcome after one year of EIBI in community agencies

Methods: We conducted pretreatment and one-year follow-up assessments of 63 children with autism (53 males) who entered EIBI in publicly funded community agencies at age 1.96-4.85 years. Intervention fidelity was monitored via direct observation of discrete trial training (DTT). Predictor variables included motor stereotypy, social approach, preverbal communication (joint attention and social orienting), and imitation. Outcome variables were IQ (Mullen Scales of Early Learning), adaptive behavior (Vineland Adaptive Behavior Scales), and autism symptoms (Autism Diagnostic Observation Schedule revised algorithms). For each outcome measure, hierarchical multiple regression was performed, entering treatment sites, intake CA, and IQ before predictors.

Results: DTT procedures were implemented with 95% accuracy, indicating acceptable intervention fidelity. Participants' IQ rose modestly from pretreatment, $M(SD) = 59.95$ (13.80), to the one-year follow-up, $M(SD) = 65.33$ (18.45), $F(1, 62) = 11.88$, $p = 0.001$, and autism symptoms decreased, pretreatment $M(SD) = 18.16$ (5.09), follow-up $M(SD) = 16.44$ (5.39), $F(1, 62) = 16.44$ (5.39), $p = 0.002$. However, adaptive behavior did not change significantly. Pretreatment CA predicted follow-up IQ ($\beta = 0.35$, $p = 0.02$) but not other outcome variables. Pretreatment IQ and motor stereotypy did not predict any outcome variable. Because social approach, preverbal communication, and imitation formed one factor, they were combined and predicted improvement in IQ ($\beta = 0.40$, $p = 0.005$, $R = .43$) and adaptive behavior ($\beta = 0.51$, $p = 0.002$, $R = .44$) above and beyond other variables, $p < .02$. However, motor stereotypy did not predict any outcomes, including increase in independently assessed stereotyped behaviors. No variables successfully predicted autism symptoms.

Conclusions: Social approach, preverbal communication, and imitation may constitute one factor (social communication) that predicts follow-up scores on developmental tests for children with autism who receive EIBI.

112.64 64 Change in Autism Classification with Early Intervention: Predictors and Outcome. E. Ben-Itzchak*[1] and D. Zachor[2], (1)*Ariel University Center/ Assaf Harofeh Medical Center*, (2)*Tel Aviv University / Assaf Harofeh Medical Center*

Background: Autism spectrum disorders (ASD) form a heterogeneous set of clinical syndromes. Great variability has been described in the severity of the social-communication symptoms, cognitive and verbal skills at diagnosis and in response to intervention, as some will show limited progress while others make rapid and remarkable gains.

Evidence regarding changes in autism severity and in ASD classification with intervention using standardized tests has been quite limited due to the scarcity of follow-up outcome studies. Previous studies looking at the stability rates of the initial diagnosis when made at two years found mixed findings. Some reported high rates of change in autism classification including moving to nonspectrum diagnosis, while others reported pronounced stability of autism symptoms and categorical diagnoses. Studies that looked for predictors of favorable outcome reported that the child's cognitive level and verbal abilities at diagnosis have a significant impact on outcome.

Objectives: The current study had three aims: 1.To characterize the changes and stability of autism diagnostic classification with intervention in very young children. 2. To examine pretreatment factors that might predict changes or stability in autism classification. 3. To compare the intervention outcome in cognitive and adaptive domains between the groups that changed or remained stable in their initial autism classification.
Methods: Sixty-nine children diagnosed with autism (clinical observation and ADI-R), aged 15-35 months (M= 25.2, SD=4.1) participated in the study. Children underwent comprehensive evaluations at pre-intervention time (T1) and after one year of intervention (T2). The evaluation included autism classification based on Autism Diagnosis Observation Schedule (ADOS), cognitive abilities (Mullen) and adaptive skills evaluation (Vineland). The sample was divided into two groups according to their autism diagnostic categories which were derived from the ADOS algorithm scores at T2. The Unchanged Group (N=53) remained in the same autism classification and the Improved Group (N=16) changed classification to Autism Spectrum Disorder (ASD) (N=14) or Off Spectrum (N=2).
Results: After one year of intervention the majority of the examined children (77%) remained with autism diagnostic classification (ADOS algorithm), 20% of the children moved to an ASD classification, and only 3% no longer met the criteria for ASD. The Improved Group had significantly better verbal scores than the Unchanged Group at T1. No significant differences between the two groups were noted in nonverbal ability, Vineland adaptive skills, child's age, parental educational attainment and parental ages. The Improved Group gained significantly more than the Unchanged Group in cognitive abilities and adaptive skills, and exhibited greater reduction of stereotyped behaviors with intervention.
Conclusions: Two distinct subtypes of autism were identified in very young children with autism. One with stable autism symptomatology, poor verbal abilities and limited cognitive and adaptive gains in response to intervention, and a second type with better baseline verbal abilities and overall better response to intervention in autism symptoms severity and in cognitive and adaptive skills.

112.65 65 Evaluation of the Autism Ontario Realize Community Potential Program. K. McFee*[1], J. H. Schroeder[1], J. Bebko[2], M. Thompson[3], K. Stoner[3], M. Spoelstra[3] and L. Verbeek[3], (1)*York University, Toronto*, (2)*York University*, (3)*Autism Ontario*

Background: For 35 years, Autism Ontario has provided support to parents of children with an ASD, promoted public awareness of ASD, supported and promoted ASD research, and worked with government leaders. The *Realize Community Potential (RCP) Program* was developed to directly support parents of children with ASD through: greater access to information, direct contact between parents and Autism Ontario chapters, improved access to experts in local communities, and increased community-based learning opportunities for children with ASD. The RCP program started as a pilot program in 6 different communities with existing Autism Ontario chapters. As part of the RCP program, Autism Ontario created a team of professionals and researchers in the field of ASD to serve as the Knowledge program evaluation team.
Objectives: Major goals of this evaluation are to determine the ability of the RCP program (1) to help to reduce stress in families of children with an ASD, (2) to provide long-term support and resources for families, and (3) to help build capacity within local chapters to support families.
Methods: A central online database was created for RCP coordinators to monitor contact with parents and families, including: Contact Log, Activity Feedback Form, and Short-term Stress survey. Baseline and follow-up questionnaires were administered to compare chapter activity before and after the inception of the RCP program. These surveys were also administered to four non-RCP Autism Ontario chapters matched on population density to serve as a comparison group.

Results: There was substantial increase in the number of chapter events offered since the inception of the RCP program. This increase was not found in the non-RCP chapters. A review of the Activity Feedback data on events offered through the RCP program collected thus far shows that 93% of participants (n = 495) felt that these events met or exceeded their expectations and 96% of participants reported that they would attend another event held by Autism Ontario, RCP program. Event topics of most interest to families included: behaviour, followed by social skills development, and communication. Interestingly, these are congruent with the three major diagnostic criteria for autism. These goals should be kept in mind when developing future events. The average number of calls to RCP chapters per month has increased 2-8 fold in all but one chapter since the program started. This was not found in the non-RCP chapters.
Data from contact logs regarding the reasons why families are contacting the RCP chapters and short-term stress are currently being collected and will be discussed. It is hypothesized that contacts of a more complex nature will be more likely to show a decrease in stress than information-seeking contacts.
Conclusions: This research is important in identifying the effective components of the RCP program to guide future program development and allocation of funding resources.

112.66 66 Is Adverse Perinatal Outcome Associated with IQ in Children with Autism Spectrum Disorders?. L. A. Schieve*[1], C. E. Rice[1], J. Baio[1], M. Durkin[2], R. S. Kirby[3], C. Drews-Botsch[4], J. S. Nicholas[5], L. Miller[6] and C. M. Cunniff[7], (1)*National Center on Birth Defects and Developmental Disabilities*, (2)*University of Wisconsin-Madison*, (3)*University of South Florida*, (4)*Rollins School of Public Health, Emory University*, (5)*Medical University of South Carolina*, (6)*Colorado Department of Public Health and Environment*, (7)*University of Arizona College of Medicine*

Background: Measured Intellectual Quotient (IQ) is associated with genetic, perinatal and postnatal factors. Studies suggest the impacts of genetic and perinatal environment on IQ are mediated by socio-economic status (SES) such that genetic and perinatal effects are most evident in mid-high SES populations without competing postnatal effects and are diminished or not observed in disadvantaged populations.

Having an autism spectrum disorder (ASD) is also highly associated with IQ deficits; 30-60% of children with an ASD have a co-occurring intellectual disability (ID). Whether environmental factors independent of a child's ASD pose additional risk for low IQ is not well studied.

Objectives: To examine associations between adverse perinatal outcomes and IQ among children with an ASD.

Methods: Singleton children born in 1994 and identified through school and health record review as having an ASD by age 8 years were selected from a US population-based surveillance network. The sample included 1,129 children from10 sites that adequately captured IQ data who were born in the same state (and linked to their birth record). Mean IQ and dichotomous IQ outcomes, ≤borderline (<85), ≤mild ID (≤70), and ≤moderate ID (<50), were examined according to whether a child was preterm (<37 weeks' gestation) or term small-for-gestational-age (tSGA, term delivery and birthweight <10th percentile for gestational age of a US referent adjusted for sex). Results were stratified by race and maternal education at birth and adjusted for child sex and ASD classification (autism; ASD-NOS; behavioral description consistent with DSM-IV but no previous ASD diagnosis/classification).

Results: Overall, mean IQ was significantly ($p<0.05$) lower in children delivered preterm (69.5) than term (74.5). Among those delivered term, mean IQ was significantly lower in those with tSGA (69.3 vs. 75.3). The preterm effect was evident across ID levels. The tSGA effect was limited to borderline-mild ID. After stratification and adjustment, the preterm-IQ association remained significant only among non-Hispanic white children with maternal education ≤high school. In this group, adjusted mean IQ was 8 points lower among those delivered preterm (65.4) than term (73.8). After stratification and adjustment, tSGA was associated with a statistically significant 8-point deficit in mean IQ (75.5 vs. 83.8) in non-Hispanic white children with maternal education >high school, and a 6-point IQ deficit that approached significance (68.4 vs. 74.5, $p=0.10$) in non-Hispanic white children with maternal education ≤high school. Non-Hispanic black children in both maternal education groups had significantly lower mean IQs than white children with little variation by preterm or

tSGA. Results were similar using SES measures based on birth census tract rather than maternal education.

Conclusions: The variation in IQ by socio-demographic and perinatal factors suggests that IQ deficits among children with ASD are partially independent of the ASD and possibly preventable. However, under-identification of minority children with higher functioning ASD might also contribute to the high proportion of non-Hispanic black children with IQ deficits. Studies of the level and effectiveness of early intervention services received by race, SES, and perinatal risk sub-groups are needed.

112.67 67 An Investigation of the Longitudinal Relationship Between Internalizing Traits and Autistic-Like Traits within a Community-Based Twin Sample. V. J. Hallett*[1], A. Ronald[2], F. Rijsdijk[1] and F. Happé[1], (1)*Institute of Psychiatry, KCL*, (2)*Birkbeck College, University of London*

Background: Autistic spectrum disorders (ASD) are characterised by impairments in social interactions, communication and the presence of repetitive and ritualistic behaviors. However, in addition to these core symptoms, a large number of children with ASD experience significant internalizing difficulties such as anxiety and depression. Very little is known about the etiological relationship between internalizing symptoms and ASD. The emergence and stability of these symptoms during childhood and adolescence also remains poorly resolved.
Objectives: The current study aimed to investigate the relationship between 'autistic-like' and internalizing traits within a population-representative sample in middle to late childhood. We assessed whether autistic-like traits had a direct influence upon later internalizing difficulties or vice versa and analysed the etiological factors influencing the longitudinal association between these traits.
Methods: Data was taken from the UK-based Twins Early Development Study (TEDS). Data for this study included approximately 5000 twin pairs assessed at ages 7 and 12. Autistic-like traits were measured using the parent-reported Childhood Asperger Syndrome Test (CAST; Scott et al 2002) at both ages and internalizing traits were measured using the emotional subscale of the Strengths and Difficulties Questionnaire (SDQ; Goodman et al 1997). A genetically informative longitudinal cross-lagged model was used to determine the etiological factors affecting autistic-like and internalizing traits at both ages. It also enabled us to disentangle the genetic and environmental influences upon the longitudinal association between these traits. Importantly, this model estimated the direct influence of autistic-like traits at age 7 on internalizing traits at age 12 and vice versa.
Results: Both traits were moderately to highly heritable at both time points, although they were largely independent with respect to their genetic influences (genetic correlation <0.18). With regard to the longitudinal results, there were bidirectional processes involved in the relationship between autistic-like and internalising traits. Autistic-like traits at age 7 significantly contributed to the emergence of internalizing traits at age 12. There was also a smaller but significant influence of earlier internalizing traits upon the presence of later autistic-like traits. Both traits showed moderate stability across the 5 year period, although etiological influences were largely specific to each time-point. There was moderate stability in the genetic influences on autistic-like traits over time.
Conclusions: Our results suggest that early autistic-like traits have a direct influence upon the presence of internalizing traits later in childhood. Furthermore, the reverse association is also supported, although to a lesser extent. That is, the presence of autistic-like traits in later childhood is also associated with earlier levels of internalizing traits. These results have important implications for our conceptualisation of the relationship between internalizing and autistic-like traits. If these symptoms serve to mutually exacerbate each other, this could also influence the timing and effectiveness of intervention methods.

112.68 68 Deviations from Normal Birth Weight and Autism Risk — California, 1989–2002. J. Zipprich*[1], G. C. Windham[2], M. Anderson[3] and J. K. Grether[2], (1)*Centers for Disease Control and Prevention & California Department of Public Health*, (2)*California Department of Public Health*, (3)*Impact Assessment, Inc.*

Background: Approximately 25,000 children born in California during 1989–2002 received services through the Department of Developmental Services (DDS) for autism, yet knowledge is limited regarding autism risk factors. Low birth weight (LBW) and preterm delivery have been linked to social and learning deficits among children; however, findings from studies of birth weight and autism are inconsistent.

Objectives: We evaluated associations between birth weight and autism risk in the California Department of Public Health statewide database, linking DDS and vital statistics data on singleton live births during 1989–2002 surviving to age 1 year.

Methods: Our study focused on children eligible for autism services after DDS evaluation (n = 23,913); all other children in the cohort (n = 7,125,777) served as control subjects. Sociodemographic factors, birth weight, and gestational age were obtained from birth certificate files. Logistic regression was used to calculate adjusted odds ratios (AORs) between autism and birth weight categories (reference, 2,500–3,999 g), controlling for maternal age, education, race, parity, sex, gestational age, year, and delivery payment type.

Results: Eleven percent of singletons were high birth weight (≥4,000 g), 3.9% LBW (1,500–2,499 g), 0.4% very LBW (VLBW, 1,000–1499 g), and 0.2% extremely LBW (ELBW, <1,000 g). AORs for autism were highest for ELBW (2.20; 95% confidence interval [CI], 1.80–2.70) and elevated for VLBW (1.20; 95% CI, 0.99–1.46), LBW (1.13; 95% CI, 1.06–1.21), and high birth weight (1.12; 95% CI, 1.08–1.16), compared with the referent.

Conclusions: Deviations from normal birth weight, particularly ELBW, were associated with an increase in the odds of autism among singleton children. Exploring this association is necessary to confirm birth weight as a predictor.

112.69 69 Intellectual Functioning and Severity of Autism Symptomotolgy Over Time. C. Shulman* and M. Ezra, *The Hebrew University of Jerusalem*

Background: A diagnosis of autism has been found to be stable over time, but there is considerable variability in the clinical profile, both between individuals with a diagnosis of autism and within each individual's unique profile over time. Because of this variability it is difficult to predict the course of autism and its distinctive expression in each individual with autism.

Objectives: The aim of the present research is to investigate the course of autism by following the changes in behavioral symptomatology, intellectual functioning and the association between them to examine the stability of diagnosis in early childhood.

Methods: Twenty-four children with autism were evaluated at two time points, the first at an average age of 4 years and 3 months and the second at an average age of 6 years. The severity of behavioral expressions of autism was evaluated using the Childhood Autism Rating Scale (CARS). Intellectual functioning was evaluated using the MSEL or the WPPSI, depending on age and level of functioning.

Results: Results revealed that the "severity of autism" was found to be stable over the period studied. In children below the average age of the sample and in children with IQ lower than 70 at initial assessment, there was an increase in severity of expression of autism symptomotology. Intellectual functioning remained stable over time, alongside changes in individual scores between the two examinations. A significant correlation emerged between behavioral expressions of autism and intellectual functioning over time. Furthermore, each variable at the first point in time was significantly correlated with the second variable at the second point in time. In other words, the more severe the behavioral manifestations of autism, the less change in IQ was observed over the period in question, and vice versa.

Conclusions: These findings provide a downward extension of previous research which studied stability of autistic features and intellectual functioning in older individuals with autism and support findings which report relative stability in the diagnosis of autism. The findings revealed that the period of early childhood in children with autism is also characterized by relative stability, of most behavioral expressions associated with autism and of intellectual functioning. Initial IQ measurement was found to be consistently and significantly associated with the changes observed over time, and with the power of the correlation between intellectual functioning and behavioral manifestations. It emerged from these results that while we may anticipate some degree of decline in intellectual functioning among children with initial IQ below 70, among those with initial IQ of 70 or above, we may anticipate stability of behavioral expressions and a modest improvement in general and performance intellectual functioning. Practically speaking, the results of this research may provide professionals who work with young children with autism a broader perspective on the disorder and

a better ability to anticipate its course and its variability over time. These factors may be taken into account both in decision making and prioritizing intervention with individuals, and in educational placements.

112.70 70 The Effect of Perceived Inclusion on Middle School Students' Attitudes and Actions toward a Peer with Autism. B. L. Kelleher* and E. R. Hahn, *Furman University*

Background: Research studying the effectiveness of inclusive educational practices has generated mixed results. Some studies have reported that students with disabilities who are educated alongside typically developing peers benefit from positive social networks (e.g., Banerji & Dailey, 1995; Kennedy, Shukla, & Fryxell, 1997). Other research, however, indicates that children with disabilities in mainstreamed educational environments may experience negative socio-emotional and health outcomes such as lower physical self-confidence, fewer close friendships, and lower rankings in classroom social status than typically developing peers (Armstrong, Rosenbaum, & King, 1992). Such inconsistent results may be due to the attitudes and actions of typically developing peers toward children with autism. Children with autism who are fully integrated, both physically and socially, with peers in general education classes may be perceived more positively by same-age peers than children with autism who are either socially rejected by typically developing peers or physically segregated from typically developing peers.

Objectives: To evaluate how different degrees of inclusion influence middle school students' attitudes and actions toward a fictional target peer with autism.

Methods: Middle school-age students viewed one of three personal websites said to have been created by Charlie, a same-age peer with autism. The websites varied in the extent to which Charlie appeared to be included in activities with typically developing peers (e.g., lunch, school dance). In the *Fully Included Condition*, Charlie was depicted as both physically and socially included in activities with peers without disabilities. In the *Partially Included Condition*, Charlie was presented alongside peers without disabilities, but he appeared to be socially rejected and ostracized by his typically developing peers. In the *Excluded Condition*, Charlie was socially included by a peer group of children with orthopedic impairments. Participants' attitudes toward Charlie were measured using a modified version of the Chedoke-McMaster Attitudes toward Children with Handicaps Scale (CATCH). Participants were also asked to predict their peers' attitudes toward Charlie. In addition to these attitudinal measures, participants were asked to divide a monetary reward between themselves and Charlie. Parent attitudes toward children with autism were measured a modified version of the Parental Attitudes toward Children with Handicaps Scale (PATCH).

Results: Preliminary results indicate that participants in the *Fully Included Condition* expressed more positive attitudes toward Charlie than participants in either the *Partially Included* or *Excluded* conditions. Furthermore, children in the *Fully Included Condition* distributed a larger portion of the reward to Charlie than participants in the other two conditions. Consistent with previous work, children in all three conditions reported more favorable personal attitudes toward Charlie than attitudes attributed to their peers.

Conclusions: Preliminary results support the hypothesis that both physical and social inclusion influence participants' attitudes and actions toward a fictional target peer with autism. These results indicate that some physically inclusive environments may not necessarily promote the social well-being of students with autism. Educators and policymakers may increase the effectiveness of inclusionary practices by working to promote greater social acceptance of children with autism by typically developing peers.

112.71 71 Designing Inclusive Educational Spaces for Children with Autism. R. Khare*[1] and A. Mullick[2], (1)*Birla Institute of Technology*, (2)*Georgia Institute of Technology*

Background: Despite the overwhelming occurrence of autism, it is by and large overlooked by the architects and designers as a condition that influences building design and excluded from building codes and design guidelines. As a result, the built environment has failed to consider the needs for users with autism. In educational spaces, the existing accessibility standards take care of physical access but children with cognitive limitations often remain unrepresented. Today with escalating incidence of autism and advent of inclusive education, it has become vital to explore the scope of environmental design for autism.
Objectives: To recognize the environmental issues

effecting performance of children with autism in educational spaces, measure the environment's impact on learning and develop guidelines for architects and designer to design autism friendly educational places. The study also explores the effect of the environment on able-bodied children for universal access and application.
Methods: There are several stages to this research and design project. To begin with 'eighteen environmental design issues' are identified based on the behavior of children and interventions adopted by the teachers and therapists. Then a three prong evaluating tool is developed to validate these issues in existing educational settings. The issues are tested in different type of educational settings that range from inclusive to specialized institutions for low functioning children with autism. The data is collected from seventeen educational settings; two preschool, five elementary, five middle and five high schools. The identified design issues are concurrently rated by twenty autism experts and thirteen regular education experts. Finally, the high performance and high rated design issues provided the foundation to develop design guidelines for autism friendly educational settings.

Results: The data on physical environment shows strong correlation between educational performance and the needs of children with autism. The environmental design issues are ranked high by educational experts who work with autistic children as well as able-bodied children. This confirms that the design issues are not only favorable for autistic kids but are also beneficial for all school children. Universal consequence of the design issues to the educational environments is furthermore defined by the mean values that establish equilibrium between environment and the demand of all users with and without autism.

Conclusions: The deficits and differences in perception of senses put people with Autism in an unnerving environment surrounded by uncertainty and unpredictability. Although designing physical environment for them requires a good understanding of individual needs, some common environmental design principles can be adopted to improve their responses to teaching and therapies.

112.72 72 From the Laboratory to the Blackboard Jungle: Conducting Technology-Based Research in the Inclusion Setting. M. Levine*[1], K. Hearsey[2], N. Woods[1], L. Kozar[2], L. Zekanovic[1] and J. Barnwell[2], (1)*SymTrend, Inc.*, (2)*University of North Carolina at Chapel Hill*

Background:

We were the first to undertake in vivo, school-based, computer-mediated treatment of social behavior of teens with Asperger's Syndrome (AS). We have completed four studies using a handheld computer-based system to enhance self-monitoring, emotional self-regulation, executive functioning and social pragmatic expression (client-funded, NIMH 1-R41-MH075162-01, NIMH 2-R42-MH075162-02). This report is a "heads-up review" for fellow investigators. It lists likely problems encountered during school-based technology research and suggests solutions. Our focus here is primarily on 1) the logistics of adhering to research protocols within a school setting and 2) dealing with computer problems and infrastructure issues.

Objectives:

The objective of this report is to help colleagues avoid the pitfalls of conducting in vivo school-based research with AS students, particularly when using computer technology.

Methods:

Middle and high schools in Massachusetts and North Carolina participated in the research. The schools were required to recruit teens 1) with a documented AS/HFA diagnosis and 2) with a full scale IQ of at least 75 documented in the last three years. In study four, student recruits in inclusion settings also had to have sufficient opportunities in their schedule for feedback and training sessions. In all cases, schools promised to provide observers and coaches. Schools agreeing to participate received training, handheld computers, software, financial support for the observers/coaches, and research staff assistance in designing specific interventions. All participating schools had excellent reputations for their programs treating individuals on the spectrum, a well-trained and dedicated special education staff, and provided better than average services to their AS/HFA students. Most of the schools served socio-economically diverse populations.

Results:

Meeting the challenges commonly encountered in the logistics of conducting technology-based intervention research requires flexible solutions for school: 1. Culture: Find a dedicated champion at the site. Understand school staff roles, responsibilities, and interrelationships. 2. Staffing: Assume there will be turnover, wide-ranging motivation and computer expertise, intermittent availability, and difficulties getting parental consent. Do not overburden your champion. Provide funding for over-time. 3. Scheduling: Plan around day-to-day variation in student schedules and attendance. 4. Research naiveté: Reinforce the use of precise, definitions of measures and the sanctity of protocols/data. Continuously monitor protocol adherence. 5. Documentation: Have alternative sources of information for incomplete records. Meeting the challenges commonly encountered with infrastructure/computers requires assertiveness to manage: 6. Equipment: Provide it all yourself. Have multiple backups readily available. 7. Space: Insist on a central location accessible to disparate programs and staff. 8. Technical barriers: Presume old wiring, limits to Internet access, barriers to wireless signals, rigid access policies, and physical abuse.

Conclusions:

Intervention research in inclusion settings requires months of planning and a large support staff. Pre-study scouting regarding the personnel and operations of participating schools is critical for integrating the research into each school's physical space, processes, and community. Adequate funding to train and support school-based personnel during off-hours and technologies for providing training and support at disparate locations are essential. Finally, be flexible and patient!

112.73 73 "Who Makes a Good Friend?" Characteristics of Peer Models for Children with Autism. J. Locke*, A. Gulsrud, C. Kasari and L. Huynh, *University of California, Los Angeles*

Background: Children with autism suffer from poor peer relationships across their life span, regardless of age and ability. Given their poor peer relationships, researchers have employed typical age mates of children with autism as part of their social skills interventions. Despite growing research that suggests utilizing typically developing peers is a critical component in teaching social skills to children with autism, less is known about these peer models.

Objectives: This study examined the characteristics of typically developing peer models.

Methods: Participants were drawn from a randomized-controlled treatment trial in the public schools in the greater Los Angeles area that examined the effects of targeted interventions on the peer relationships and social networks of 60 elementary-aged children. Of the 838 typically developing children who consented to be in this study, 107 children (52 females and 55 males), mean age 7.92 years old (SD=1.42) were selected as peer models and participated in a 12-session 6-week intervention. All children were nominated by their teachers to be peer models for children with autism included in regular education in 1^{st}-5^{th} grade. Teachers were told to select peers who are understanding, willing to help, and patient and need not be the most popular children in the classroom. Children completed a friendship survey that was coded for children's friends, connections, and rejections following the methods outlined in Cairns and Cairns (1994) as well as a loneliness measure that assesses feelings of loneliness in relation to a dyad or group (Hoza, Bukowski, & Beery, 2000).

Results: A descriptive analysis demonstrated that typical peer models rejected very few children in their classroom, mean = 2.36 (SD=2.50) and infrequently received rejections by other children, mean =1.09 (SD=1.32). Overall, 88.8% of the peer models were secondary or nuclear in their classroom social network ratings. A univariate analysis of variance indicated that typical peer models had significantly higher social network ratings than typically developing children who were not selected as peer models, $F(1, 838) = 4.65$, $p<.05$. In addition, a univariate analysis of variance indicated that typical peer models reported less loneliness than non-peer models, $F(1, 735) = 4.15$, $p<.05$.

Conclusions: Overall, peer models had higher social network ratings and reported fewer feelings of loneliness than non-peer model classmates. These results suggest that typical peer models for children with autism are more socially connected in their classroom and appear more self-assured in their feelings regarding relationships with others. Utilizing peer models that are more connected to other children in the classroom may be instrumental in social skills interventions for

children with autism. Their social standing may influence other children's perceptions of children with autism in terms of acceptance and social engagement.

112.74 74 Do Motor Difficulties Contribute to Peer Rejection and Social Isolation in 'High-Functioning' Children with Autistic Spectrum Disorders?. M. Murin*[1], L. Slator[1], W. Mandy[2] and D. H. Skuse[3], (1)*Great Ormond Street Hospital for Children*, (2)*University College London*, (3)*Institute of Child Health*

Background:

Motor difficulties are described, by DSM-IV-TR, as possible contributors to peer rejection and social isolation among children with Asperger syndrome. No previous study has explicitly measured the independent contribution made by motor competence or clumsiness/dyspraxia to peer relationships among children with 'high-functioning' autism, Asperger syndrome, or other pervasive developmental disorders.

Objectives:

We aimed to examine the impact of measures of gross and fine motor skills, current clumsiness and dyspraxia, upon parent and teacher and reports of peer relationships and social rejection, in a large heterogeneous sample of 'high functioning' children with Asperger syndrome, autism, or PDD-NOS.

Methods:

Data from parental report were analysed for a sample of 303 children (4-16 years, mean age 9.0 yrs) from London, UK, which had been subject to comprehensive and standardized autism assessments (including ADI algorithm, ADOS). All subjects had normal-range intelligence. Diagnoses were defined according to DSM-IV-TR criteria, and comprised autism (N=106), Asperger syndrome (N=97), PDD-NOS (N=100). Measures of motor competence included developmental motor milestones, current fine and gross motor skills, and a dyspraxia/clumsiness index. Domains were derived by principal components analysis of a validated parent-report scale. Peer relations were measured by parent/teacher rated Social Difficulties Questionnaire peer relations score, and other standardized measures of peer acceptance or rejection.

Results:

Children with autism had similar gross motor skill deficits to those with Asperger and PDD-NOS. Fine motor skill deficits were significantly worse in both autistic and Asperger groups, in relation to PDD-NOS. Our measure of dyspraxia/clumsiness also indicated relatively more impairment in the autistic group than other diagnostic categories.

We tested the hypothesis that, controlling for the severity of non-motor autistic symptoms in all three domains of autistic disorder (i.e. ADI-R algorithm scores for qualitative abnormalities in social interaction, qualitative abnormalities in communication and restricted, repetitive and stereotyped patterns of behaviour), motor competence would account for a significant proportion of the variance in measures of peer acceptance. We found that impairments in gross motor skills (but not fine motor skills, or dyspraxia/clumsiness) independently predicted the degree of peer relationship difficulties, but the size of the effect was small (standardized beta, 0.14, p=0.018). There was no moderating effect of gender. The impact of the motor problems was similar in all three categories of diagnosis.

Conclusions:

Motor skill deficits, and dyspraxia/clumsiness are similar in children with 'high-functioning' autism and Asperger syndrome. Such difficulties are commonly assumed to contribute to peer-relationship problems, independent of the severity of autistic symptoms that contribute to phenotypic definition. Ours is the first study to test this hypothesis in a large sample, using standardized measures. We found a small but significant impact, relating significantly and exclusively to gross motor abilities.

112.75 75 Towards Designing An Interactive and Intelligent Tool for Social Skill Development of Individuals with HFA. J. C. C. Gillesen[1], R. I. Arriaga*[2] and M. Riedl[3], (1)*Eindhoven University of Technology*, (2)*Georgia Institute of Technology*, (3)*Georgia Tech*

Background:

Research and anecdotal evidence suggests that individuals with high functioning autism (HFA) respond well to social skills instruction and related applications, such as Social Stories. These techniques can be used to introduce socially appropriate behaviors in specific circumstances. However, individuals with ASD have a hard time adapting to unexpected events (e.g. when things

"go wrong"). They often respond to these events with behavior that is not socially acceptable or age-appropriate. These inappropriate behaviors limit their social opportunities, which negatively impact their quality of life.

Objectives:

We see an opportunity for technology to provide custom generated scenarios for the individual to experience social situations and appropriate responses to unexpected events. Technology can also assist and support reflecting on those experiences. Finally, it can gather data to assess the individual's skill level and adjust the scenarios appropriately. A long term goal is to have the assessment and scenario generation automated via artificial intelligence.

Methods:

A pilot study was conducted in the (8 boys/2 girls, age 7-12, IQ 67-99). Children were presented with a bridge crossing scenario through an interactive computer animation (ICA, completed twice) and were then presented with a paper prototype (PP, completed once) to retell the experience. All sessions were video-taped.

Results:

In the ICA study we found that six out of nine children were aided by the rehearsal feature. In the PP study the children used different perspectives to tell the story, and used a rich set of interaction modes with the given pieces. Two different types of prompts were required: One to continue the story and one to elaborate on the details.

Conclusions:

After a more in depth literature review and input from experts in the clinical field, we are now starting the second iteration of the project. The first step is to prototype a set of scenarios that will connect to the personal experience of our defined user group, which will run in a software demo. For the reflection method we will develop a set of puzzle pieces which contain the same pictures as seen in the scenario. These puzzle pieces can then be sequenced in the right order, providing visual feedback via lights, as a reward and as a prompt to continue the activity. In addition, sound modules will contain the dialog of the scenario or allow for the user to record short messages with each picture.

We see an opportunity for technology that may greatly benefit important skill development for high-functioning children with autism. We concluded that it is possible to create an ICA with the flexibility of the PP in an intelligent system that will provide the necessary prompting. With our system there is the freedom to practice different outcomes, learn proper behaviors by increasing in levels and generalize the learnt skills to other contexts. We will be conducting a pilot study of the new system in early January.

112.76 76 Dissemination of Evidence-Based Practice: Can We Train Therapists from a Distance?. L. A. Vismara*[1], G. S. Young[2], A. Stahmer[3], E. McMahon-Griffith[4] and S. J. Rogers[1], (1)*M.I.N.D. Institute, University of California at Davis*, (2)*M.I.N.D. Institute, University of California at Davis Medical Center*, (3)*Rady Children's Hospital*, (4)*University of Alabama at Birmingham*

Background: Although knowledge about the efficacy of behavioral interventions for children with autism is increasing, there is little research on the effectiveness and transportability of empirically supported models in diverse community settings.

Objectives: The current study conducted an effectiveness trial to compare distance learning versus live instruction for training community-based therapists to implement the Early Start Denver Model (ESDM), a developmental, relationship and behavioral-based method for use with infants and toddlers with Autism Spectrum Disorder.

Methods: The following three training conditions were provided sequentially to teach direct intervention and parent coaching of the ESDM: (a) self-instruction with the training materials using print and video materials provided on a DVD; (b) didactic workshops with direct instruction and group training exercises; and (c) team supervision for specific discussion of training cases.

Results: Findings revealed: (a) distance learning and live instruction were equally effective for teaching therapists to both implement the model and to train parents; (b) didactic workshops and team supervision were required to improve therapists' skill use; (c) significant child gains occurred over time and across teaching

modalities; and (d) parents implemented the model more skillfully after coaching.

Conclusions: Family characteristics, therapist variables, and contextual factors will be examined to determine whether modifications from the original efficacious intervention model are needed for the generalization of positive treatment effects to large community populations. Findings are also discussed in terms of the circumstances under which the ESDM is effective and for whom.

112.77 77 Enriched Home Environment: a Model & Intervention to Facilitate Participation in Children with ASD. D. Sood*, S. Iovaldi and J. Bunn, *University of Missouri*

Background:
Enabling childhood participation in home activities requires complex interactions between the child and a stimulating ecology. Home environment plays a vital role in child development. Children with Autism Spectrum Disorder (ASD) may have lower participation in home activities. This study explores a measurement and an intervention model to understand the relationship between a child with ASD and a stimulating ecology as defined by an enriched home environment.

Objectives:
Examine the relationship between participation of children with autism, parenting stress and the enriched home environment and to identify key factors in the environment that influence the child's participation in home activities.
Develop a measurement and an intervention model of an enriched home environment.
Develop a Home Environment Checklist (HEC) to assess the level of environmental complexity present in the home environment of children with ASD.
Implement an eight-week home modification program to provide learning, sensory and a socially stimulating environment.
Identify changes in participation of children with ASD in home activities following an eight-week intervention program.

Methods:
To examine the relationship between participation of children with ASD and environmental factors (parenting stress and enriched home environment), 22 Children with a diagnosis of ASD ages 3 to 6 years were recruited for the study. Home Observation for Measurement of Environment (HOME) and Preschool Activity Card Sort (PACS) assessments were performed. The parents filled the Parenting Stress Index (PSI), and Social Responsiveness Scale (SRS). A spearman rank coefficient and a multiple regression analysis was used to analyze the relationships.
To implement an eight-week home modification program, 2 children were recruited. Pre intervention data was collected using the Home Environment Checklist (HEC), Preschool Activity Card Sort, Parenting Stress Index, and Sensory Profile. Following an eight-week home modification program, post intervention data was collected using the Preschool Activity Card Sort. A percentage change was documented to analyze the changes in participation in home activities following an eight-week home intervention.

Results:
Significant correlations were found between parenting stress, the characteristics of the home environment and participation patterns of children in home activities. Based on multiple regression analysis, the variance in participation in low demand leisure activities of children with autism was predicted by the availability of the learning materials in the home and the parenting stress after controlling for the severity of child diagnosis. Also an increase in the scores on the preschool activity card sort following an eight-week home modification intervention were reported for both the children, though these results were not statistically significant.

Conclusions:
The results of the study helped in understanding the environmental factors that influence participation of children in home activities. Also, the Home Environment Checklist can be used to measure the level of environmental complexity in home environment of children. Providing an enriched home environment to children with ASD can improve their participation in home activities. Overall, this study provides a guideline to develop a measurement and intervention model to develop enriched home environment for children with ASD.

112.78 78 CARE for the Caregivers: Supports for Better HEALTH Outcomes in Mothers of Children with Autistic Spectrum Disorder. P. S. Hutchinson* and S. E. Bryson, *Dalhousie University/IWK Health Centre*

Background: Few parents are prepared for the unrelenting demands of raising a child with autism. Mothers of children with autism are at particularly high risk for compromised health

outcomes (Hastings, 2003). While a plethora of research exists on maternal stress and increased rates of maternal depression, virtually nothing is known about specific supports and services that contribute to *better* health outcomes in mothers. Objectives: To 1. identify informal and formal supports associated with *better* health outcomes (depression, anxiety, and personal growth) in mothers of children with autism; and 2. determine whether informal/formal supports mediate or moderate the relationship between child disruptive behaviour and mothers' health. Methods: Participants included 94 mothers (M age = 41.18, SD = 7.13) of children with autism (M age = 10.7, SD = 4.91). Mothers completed a series of questionnaires on demographics, child disruptive behaviour (Developmental Behaviour Checklist), supports (Family Support Scale) and maternal mental health outcomes (Hospital Anxiety and Depression Scale and Positive Contributions Scale).
Results: Preliminary analyses reveal that 71 percent of mothers reported anxiety and 31 percent of mothers reported depression, both in the clinical range. Mothers of younger children reported higher levels of depression ($r = -.35$, $p < .01$). Children's disruptive behaviour was related to mothers' anxiety ($r = .25$, $p < .05$) and depression ($r = .3$, $p < .05$) but not to supports received. Mothers with lower depression scores reported more helpful *informal* (i.e., family and community; $r = -.41$, $p < .01$) and *formal* (e.g., professional) support ($r = -.24$, $p < .05$). Mothers with higher education reported less child disruptive behaviour ($r = .28$, $p < .01$), more *informal* support ($r = .34$, $p < .01$), and more helpful community support ($r = .23$, $p < 05$). More helpful community support was also related to mothers' reporting more positive personal growth ($r = .30$, $p < .01$). Regression and mediator/moderator analyses will address the question of how supports might predict/influence mothers' health.
Conclusions: As predicted, children's behavioural difficulties were related to mothers' depression and anxiety. Counter to predictions, children's disruptive behaviour was not related to informal or formal supports. Instead, mothers' with better health and higher education received more helpful informal and formal supports. In contrast, "high-risk" mothers, those with younger children, poorer health and/or lower education, were not as likely to access supports associated with better health. Discussion focuses on the critical question of how supports and services might more effectively address the needs of mothers caring for children with autism.

112.79 79 Daily Stress and Negative Affect among Mothers of Children with Autism Spectrum Disorder: The Role of Psychological Resilience. N. Ekas* and T. L. Whitman, *University of Notre Dame*

Background: As a result of the challenges associated with raising a child with autism spectrum disorder (ASD), mothers typically report elevated levels of psychological distress. Studies have found that individual differences in psychological resilience contribute to successful adaptation to stress. Psychological resilience includes personality variables such as optimism, locus of control, and satisfaction with life.

Objectives: To investigate the relationship between stress and negative among mothers of children with ASD utilizing a daily diary methodology. In addition, the protective role of global psychological resilience will be examined to explain the individual differences in the stress and negative affect relationship.

Methods: Participants consisted of 49 mothers with a child with ASD. Mothers completed the following questionnaires on a daily basis for 30 consecutive days: Positive and Negative Affect Scales (PANAS), Daily Negative Life Events Scale, Daily Autism-Related Stress Scale, Life Orientation Test (LOT), Satisfaction with Life (SWL), and Control of Internal States (CIS).

Results: Analyses revealed that daily negative affect was associated with daily life stress ($r = .67$, $p < .001$) and daily autism-related stress ($r = .43$, $p < .01$). Global optimism ($r = -.36$, $p < .01$), control of internal states ($r = -.294$, $p < .05$), and life satisfaction ($r = -.32$, $p < .05$) were significantly related to daily negative affect. Simple linear regression analyses also found similar results. Results of the moderation analyses found that the interactions of daily life stress and global optimism ($B = -.15$, $p < .05$) and daily life stress and control of internal states ($B = -.12$, $p < .001$) were significant. The interactions involving daily autism-related stress and global psychological resilience variables were non-significant. Multilevel modeling using Hierarchical Linear Modeling software will be conducted to confirm these preliminary findings.

Conclusions: Findings confirm that daily stress predicts daily well-being among mothers of

children with ASD. Specifically, higher levels of both life and autism-related stress predict higher levels of negative affect. Further, we also found that global psychological resilience can help protect against the negative effects of stress. Mothers who report high levels of daily stress and high levels of optimism report lower levels of negative affect as compared to those who report high levels of daily stress and low levels of optimism. In addition, mothers who report high daily stress and high global control report lower levels of negative affect as compared to those with high daily stress and low control. These findings suggest that dispositional psychological resilience may be beneficial for chronically stress mothers.

112.80 80 Awareness of Friendships and Rejections: a Comparison Between Children with Autism Spectrum Disorders and Children with Typical Development. E. H. Ishijima*, M. Kretzmann, J. Locke and C. Kasari, *University of California, Los Angeles*

Background: Individuals with Autism Spectrum Disorders (ASD) have difficulties with social interactions. These difficulties may stem from an impaired self- other-awareness, the ability to have an introspective awareness of her/his own thoughts and to impute the mental states of others.

Objectives: This study examines whether children with ASD are more rejected by classmates as compared to their typical peers. Second, our study examines the social awareness in terms of friendships and rejections of children with ASD as compared to their typical peers.

Methods: Participants were drawn from a randomized-controlled treatment trial in schools in the greater Los Angeles area that examined the effects of targeted interventions on the peer relationships and social networks of 60 elementary-age children with autism. There were 16 children in first grade, 17 in second grade, eight in third grade, 11 in fourth grade, and eight in fifth grade. Children identified with ASD were from diverse ethnic backgrounds (46.7% Caucasian, 5% African American, 21.7% Latino, 16.7% Asian, and 10% Other) and were predominantly male (90%). All were fully included in regular education classrooms and were an average of 8.14 years old (SD =1.56), with an average IQ of 90.97 (SD =16.33). Measures included a friendship survey that determined children's friends, social connections, and rejections following the methods outlined in Cairns and Cairns (1994). Participants were asked to name their friends in their classrooms, and to identify kids they did not want to hang out with. Awareness in this study was defined as the congruency between the way a child perceived her/his social status with classmates versus the way classmates perceived their social status with that child.

Results: Paired-sample t-tests revealed that children with ASD are less likely than their typical counterparts to have their "best friend" nomination reciprocated, $t(59) = 4.09$, $p < .001$. Furthermore, children with ASD are more likely than their matched peers to be completely overlooked by classmates that they listed as "best friend", $t(59) = 3.423$, $p = .001$. In regards to rejection, although children with ASD are more likely to be rejected as compared to their typical peers, $t(59) = 2.82$, $p < .01$, both groups were similar in their reciprocations of rejection, $t(59) = 1.26$, $p = .211$.

Conclusions: Our results show that children with ASD are more likely than their typical peers to inaccurately assume that they are friends with classmates. Although having the belief that they have friends may be helpful to isolated children with ASD, they are more often rejected than their matched peers. Furthermore, children with ASD are just as aware of their rejections as compared to their typical peers, which suggests that the impairment in social awareness of children with ASD is in terms of friendships and not pronounced in terms of rejection. Future studies should examine whether accuracy in social awareness, in the contexts of friendships and rejections, serves a protecting role from feelings of loneliness in children with ASD.

112.81 81 The Need for Social Belonging in Individuals with Extreme Autistic-Like Traits. L. A. Harborow*, V. Locke and M. Maybery, *University of Western Australia*

Background:

Individuals on the autism spectrum are often characterised by a lack of interest in social interactions. However, previous research is yet to determine whether this apparent lack of interest reflects a decreased need for social belonging. It has also been suggested that individuals in the general population who self-report autistic-like traits on the Autism Spectrum Quotient (AQ) may share characteristics of individuals with a clinical

diagnosis of the disorder. A body of social psychology literature argues that the need for social belonging is a universal human motivation. Furthermore, recent research has demonstrated that this fundamental need for social belonging can be threatened through acts of social ostracism.

Objectives:

The current research examined psychological reactions to an act of social ostracism in individuals scoring on the extremes of the AQ in order to investigate the need for social belonging in individuals reporting high levels of autistic-like traits. Lack of evidence of need threat following ostracism may indicate that the need for social belonging is less pervasive in individuals with elevated autistic-like traits.

Methods:

Undergraduate psychology students with extreme scores on the AQ (high score indicates extreme autistic-like traits and low score indicates lack of autistic-like traits), were either ostracised or included in an online ball toss game (Cyberball). Previous research has demonstrated that ostracism causes reductions in mood and elevated ratings of threat to four fundamental needs: social belonging, control, self-esteem and meaningful existence. Participants scoring high on the AQ were expected to report less reduction in self-reported mood and less threat to fundamental needs, in particular social belonging, following ostracism.

Results:

Contrary to expectations, high AQ participants reported a comparable change in threat to social belonging relative to low AQ participants following ostracism. Interestingly high AQ participants reported higher baseline self-reported arousal, which was heightened further following either ostracism or inclusion in the Cyberball paradigm, relative to low AQ participants.

Conclusions:

Results indicate that the need for social belonging is intact in individuals with extreme autistic-like traits. Perhaps where such individuals differ is in their acquisition of the social skills necessary to meet this fundamental need.

112.82 82 Social Preferences in High Functioning Autism: The Role of Theory of Mind and Empathy. V. Pelligra*[1], G. Doneddu[2], A. Isoni[3], P. M. Peruzzi[2] and R. Fadda[1], (1)*University of Cagliari*, (2)*A.O.B. (Azienda Ospedaliera Brotzu)*, (3)*University of East-Anglia*

Background: Economists explain other-regarding behavior using the idea of 'social preferences' and distinguish between 'outcome-based strategies' (Fehr & Schmidt, 1999), in which agents focus mainly on the material consequences of their actions, and 'intention-based strategies' (Rabin, 1993), in which agents react to each other's perceived intentions. One way to distinguish the relative success of the two strategies in predicting actual choices is to compare the behavior of Autism Spectrum Disorders (ASD) and Normally Developing (ND) individuals, in situations in where both outcomes concern and intention-detection could be important.
Objectives: While ND children acquire full mentalizing and empathising abilities quite early, subjects affected by ASD usually show difficulties in ascribing and understanding others mental states (Baron-Cohen, 1995; Cohen and Volkmar 1997; Gillberg, 1999). For this reason the analysis of their behaviour in strategic situations can be useful in understanding the nature of social preferences.
Methods: 18 participants with ASD (all males; aver.chron.age=15 yrs;DS=3;4; aver.IQ=84; DS=10) and 41 ND children (all males; aver.chron.age=10;5yrs; DS=9 mths) were asked to play four mini-ultimatum game (mini-UG) di Falk, Fehr e Fischbacher (2003). The participants were also tested for mentalizing abilities with a second order false belief task (Wimmer & Perner, 1985) and with the Cambridge Empathy Quotient (Baron-Cohen and Wheelwright, 2004).
Results: Children with ASD were lower than NDs in empathy scores (ASD aver. EQ scores=32.33; DS=5.61 - ND aver. EQ scores =40.41; DS=7.52 – $z=3.73$; $p<0.01$) and only the 44% of them passed the false belief task, while the 100% of NDs succeeded in that test (chi square = 148.24; df=1; $p < 0,01$). ND subjects follow the same pattern already observed in adults in previous research, characterized by positive and negative reciprocity and inequality-aversion, while ASD subjects show negative reciprocity and greater levels of inequality-aversion ($z =-2.67$, $p< 0,05$). ASD subjects with a lack of ToM are not susceptible to positive reciprocity ($z =-2.56$, $p< 0,05$).
Conclusions: The other-regarding behavior of

children with ASD can be explained mainly by inequality-aversion that in this population was not related with empathy, possibly because ASDs referred inequality to their materials gains and not the benefit of the others. Furthermore, a lack of intention-detection was involved in perseverant negative reciprocal choices. These findings suggest that the effect of perceived intentions in motivating reciprocal behavior is not as linear as standard economist rational choice theory suggests but needs to be further investigated.

112.83 83 Shyness, Sociability, and Social Dysfunction in Adults with Autism. I. E. Drmic*[1], S. E. Bryson[2], M. K. Jetha[3] and L. A. Schmidt[4], (1)*Hospital for Sick Children*, (2)*Dalhousie University/IWK Health Centre*, (3)*Brock University*, (4)*McMaster University*

Background: Although impairment in social functioning is a core characteristic of autism spectrum disorder (ASD), little attention has been paid to whether individual differences in personality may underlie such impairments and account for the variability in social outcomes. One logical personality trait to examine is shyness. Schmidt, Polak and Spooner (2005) have proposed a vulnerability model in which early biological and behavioral antecedents of shyness identifiable in infants and young children are linked to sensitivity of forebrain limbic and frontal cortical areas, and produce dysfunction in one's ability to regulate social stress. Objectives: We examined the relation between features of autism and shyness, sociability, and social dysfunction. Methods: High-functioning adults (n = 29) with autism/ASD and matched controls (n = 29) completed questionnaires examining ASD features (Autism Spectrum Quotient; Baron-Cohen et al., 2001), components of personality (Cheek and Buss Shyness and Sociability Scale; Cheek & Buss, 1981; and Eysenck Personality Questionnaire-Revised Short Version; Eysenck & Eysenck, 1991), and anxiety symptoms (Beck Anxiety Inventory; Beck & Steer, 1990). Results: As expected, individuals with ASD had significantly higher scores on the Autism Spectrum Quotient than controls, indicating behavior characteristic of ASD. Individuals with ASD also reported a significantly higher degree of shyness (p = .0005) and neuroticism (i.e., a predisposition to anxiety; p = .002), and a lower degree of sociability (p = .041) and extraversion (p = .047) than individuals in the control group. Correlations among measures (all p's < .05) within the ASD group revealed that shyness was associated with less sociability (r = -.45), poor social skills (r = .68), poor communication skills (r = .53), difficulty switching attention (r = .47), anxiety symptoms (r = .39), high neuroticism (r = .60) and low extraversion (r = -.69). Difficulty switching attention in ASD was also associated with poor communication (r = .47) and anxiety symptoms (r = .54). Conclusions: Individuals with ASD reported significantly greater shyness and reduced sociability than controls. We also provide evidence that within the ASD group there is a link among trait shyness and impairments in social interaction and communication, anxiety, and difficulty switching attention. Individual differences in early-developing personality traits may not only explain the variability in social outcomes in ASD, but also serve to identify early in life those at highest risk for co-morbid anxiety and mood disorders.

112.84 84 Processing of Affective Information in Face, Voice, and Situational Contexts in Children with Autism Spectrum Disorders. L. M. Black*[1], J. P. H. van Santen[1], R. Coulston[1], J. de Villiers[1] and R. Paul[2], (1)*Oregon Health & Science University*, (2)*Yale University School of Medicine*

Background: Impairment in social interaction is a core symptom of autism spectrum disorders (ASD), and weak processing of nonverbal affective information is considered a critical skill impacting social reciprocity. Although there have been numerous studies testifying to weaknesses in facial affect recognition, both at behavioral and neurological levels, there have been few studies documenting that children with ASD also have difficulties understanding the feelings of others as conveyed through vocal prosody. Objectives: The purpose of the study was to measure sensitivity to affective expressions in multiple non-verbal modalities -- facial, vocal, and situational -- in children with ASD vs. Typical Development (TD). Methods: Seventy nine children ages 4-8 underwent diagnostic and neurocognitive assessments enabling classification of 37 children into the ASD group, 42 children into the TD group, and neuropsychological characterization of the ASD children. Affect measures included a computerized version of Facial and Situational Affect Matching Tasks (Fein, et al., 1985; 1992) in which participants pointed to one of four affects, using a computer touch screen, that matched the facial emotion of a targeted figure (Facial Affect Task) or the emotion conveyed by a person, with face covered up, engaged in a conventional social situation (e.g., a child at a birthday party) (Situational Affect Task). In the Vocal Affect Recognition Task, participants pointed to one of

four affects that matched the feeling conveyed in a verbal communication. Professional actors, male/female/adult/child, were asked to read neutral sentences (i.e. "it is round") in context to help elicit the emotion (i.e., scared: "I see what's hidden—it is round! It's a bomb!") with utterances then extracted from context. Using multiple speakers ensured that deep processing of affect was required and not just recognition of repetitive acoustic patterns of one speaker. Practice items established that instructions were understood, and all subjects were trained to 100% mastery on response options. Results: Data were analyzed using Analysis of Covariance, with age as covariate. Compared with the ASD group, the TD group performed significantly better ($p<0.001$) on Vocal Affect Recognition (63% vs. 48%), Situational Affect (78% vs. 58%), and Facial Affect (78 vs. 65%). On two control tasks, the TD group performed somewhat better on a Facial Recognition Task ($p<0.025$, 80% vs. 69%), and not significantly better on an Object Recognition Task ($p>0.15$, 77% vs. 71%). Planned comparisons showed 2-way interactions ($p<0.015$) between Group (ASD vs. TD) and Task (average of the three Affect Tasks vs. Object Recognition Task) and between Group and each individual affect task vs. the Object Recognition Task, indicating between-group differences on the affect tasks could not be attributed to a broad visual processing deficit. Conclusions: Findings confirm prior evidence for significantly weak recognition of facial affect and situational affect in children with ASD (Fein, et al.; Ozonoff, et al.). Significant difficulties also found in this study to discern the emotional tone of verbal communications adds importantly to our understanding of the social interaction and communicative reciprocity difficulties of children with ASD.

112.85 85 Assessment of Empathy in Pervasive Development Disorder through Tasks of Judging Basic Facial Expressions. C. S. de Paula*, A. A. Vinic and J. S. Shwartzman, *Universidade Presbiteriana Mackenzie*

Background: Invasive Development Disorders (IDD) are a group of conditions characterized by the onset of lags and impairments in the development of social, communication and behavioral skills during infancy. The empathy capacity prejudice has been indicated as an endophenotype characteristic of IDD.

Objectives: The present study evaluates and compares empathy in people with IDD and a control group through a task of judging basic facial expressions that are contained in an Empathy Card-deck.

Methods: Seven male participants with IDD, aged between 6 and 15 years, a minimum IQ of 70 (Wisc III) and all fulfilling criteria for IDD diagnosis (DSM IV) were evaluated through an Empathy Card-deck, an instrument developed by the researcher.

Results: The IDD group erred significantly more than the control group in judging the card-deck of basic facial expression photos ($p< 0.001$), in the card-deck of drawings ($p=0.007$) and in both tests when the total performance was analyzed ($p< 0.001$). There was a significant difference between the control and IDD groups in the expression of doubt ($p=0.031$) and disgust ($p=0.005$) in the Drawings Card-deck, and in the expression of disgust ($p=0.005$) in the Photo Card-deck, always with a greater error index for the IDD group. When analyzing the performance in Photos and Drawings together, there is a statistically significant difference between expressions of doubt ($p=0.012$), disgust ($p<0.001$) and surprise ($p=0.006$).

Conclusions: The results obtained reinforce the findings of previous studies about empathic capacity prejudice in individuals with IDD.

112.86 86 Can Children with Autism Recognise Emotions from Moving Faces?. S. Garib-Penna*, D. G. Moore and R. George, *University of East London*

Background: Recent studies have suggested that impairments shown by children with autism in recognising emotions may be a consequence of cognitive problems, such as motion processing, rather than a result of a specific and widespread affective disorder. To our knowledge, the majority of studies investigating emotion recognition abilities in children with autism have done so by eliciting responses from children with static images of emotional faces. These studies have yielded somewhat conflicting results. In light of recent evidence that children with autism may have motion processing difficulties, and that when interacting with others in real-life situations, facial features and often the head are moving, it is important to investigate emotion recognition abilities in non-static stimuli.

Objectives: We presented preliminary data at last year's IMFAR conference (2008) showing that

children with autism performed differentially when presented with emotions and vowels in faces moving at different speeds. This year, we present data from a follow-up study which explores whether the amount and type of movement presented in emotional and non-emotional faces can determine performance in emotion recognition in the same sample of children with autism.

Methods: Children with autism aged 8 to 14 years; children with moderate learning difficulties matched to the autism group on chronological and verbal mental age; and verbally-matched typically developing children aged 4 to 7 years took part in this experiment. Children were asked to undertake an emotion recognition task, in which they had to match dynamic videos of emotions with corresponding photographs. The *amount and type of movement* presented in dynamic facial stimuli was manipulated. Specifically, in the first condition, videos of actors moving their facial features naturally to convey an emotional expression were presented; whereas in the second condition, the videos from the first condition were edited to comprise a snapshot effect, rather than a smooth natural movement. This snapshot effect is intended to mimic the blinking strategy that people with autism have reported to use when "their world is moving too fast". The third and fourth conditions were the same as the first and second conditions with an added motion element: actors moved their heads from one profile to the other whilst portraying the emotions, either in a continuous movement or with a snapshot effect. The non-emotional control task consisted of silent vowel production.

Results: and Conclusions: Analyses are currently being conducted and will be ready for presentation at the IMFAR conference.

112.87 87 Facial Affect Recognition in Individuals with Autism Spectrum Disorders. L. Guy*[1], D. Glass[2], K. Rockers[1], O. Ousley[3], K. Kulka[1] and A. Pakula[1], (1)*Emory University School of Medicine*, (2)*Marcus Autism Center*, (3)*Emory University*

Background: Deficits in social cognition (i.e., the ability to process social information) are core symptoms in autism spectrum disorders (ASD). One aspect of social cognition involves perception and recognition of different facial expressions. Abnormalities in facial information processing have been described in the literature for ASD. The inability to accurately identify emotion shown on faces impacts social communication because much information about the intended message is conveyed nonverbally. A weakness in this area can affect reciprocal social interactions and lead to interpersonal difficulties.

Objectives: The purpose of this study was (1) to examine the ability of individuals with ASD to discriminate among common facial expressions using the Affect Recognition subtest of the NEPSY-II, a recent measure with limited empirical data on an ASD population, and (2) to see if identified deficits are correlated to real-life behavior reported by parents.

Methods: Study participants included 43 children ages 5-17 years who participated in the Simons Simplex Collection, a North American multiple site, university-based research study, which collects genetic and phenotypic information from families that have only one child with an ASD. The phenotypic battery includes administering a number of measures including the Autism Diagnostic Interview – Revised (ADI-R), Autism Diagnostic Observation Schedule (ADOS), an intelligence test, and parent and teacher report versions of the Social Responsiveness Scale (SRS). For the present study, an additional measure was collected, the Affect Recognition subtest of the NEPSY-II. This task involves the presentation of pictures of children's faces and the examinee has to either "decide if two expressions are the same or different, determine which two faces have similar expressions, or identify two children with expressions that match a third child's face" (Korkman et al., 2007). The emotions presented include happy, sad, neutral, angry, disgust, and fear. A total standard score was generated as well as the number of errors for each emotion.

Results: Data analysis will evaluate participants' total standard scores on the Affect Recognition subtest to determine the presence of deficits. This will provide empirical data on how an ASD cohort performs on the Affect Recognition subtest. The second aspect of data analysis will explore whether the score on the NEPSY-II Affect Recognition subtest correlates with parent report of facial expressions on select items of the ADI-R (e.g., social smiling, range of facial expressions used to communicate, and inappropriate facial expressions) and with the Social Communication domain of the SRS questionnaire. The NEPSY-II score will also be compared to the observed behavior on the ADOS (e.g., facial expressions directed to others and empathy/comments on others' emotions).

Conclusions: The findings from this study will provide additional information regarding the phenotypic expression of ASD. In particular, it will add to our understanding of the social perception skill of facial affect recognition, which is important for successful interpersonal interactions. The identified deficits in facial affect recognition will be compared to real life behavior reported by parents on standardized questionnaires and behavior observed during testing.

112.88 88 "Who Said That?" Affective Face and Voice Matching in Adolescents with Autism. R. B. Grossman*, M. Kennedy and H. Tager-Flusberg, *Boston University School of Medicine*

Background: Individuals with autism spectrum disorders (ASD) have deficits in the core areas of social interaction, communication, and repetitive/stereotyped behaviors. Studies also describe difficulties interpreting affective information from facial expressions and tone of voice (prosody), a skill requiring communicative and social competence; however, the evidence is often contradictory. Some studies using basic, strong emotions found preserved competence (Grossman, Klin, Carter, & Volkmar, 2000), while others, using more subtle emotional states described deficits in prosodic and facial affect recognition (Golan, Baron-Cohen, & Hill, 2006).

Objectives: The purpose of the present study was to bridge the gap between these conflicting data by using prosodic stimuli and facial expression contrasts that range from subtle to intense, in order to determine at which point on that continuum – if any - individuals with ASD show reduced competence in non-verbal affect recognition.

Methods: Participants were 22 adolescents with ASD and 22 typically developing (TD) peers matched on age, IQ, sex, and receptive vocabulary. We presented 8 semantically neutral sentences (e.g. "She bought a lot of soda"), spoken in two positive emotions (happy, surprise) and two negative emotions (anger, sadness) at two intensity levels (weak, strong) each, for a total of 64 stimulus sentences. Following each sentence, participants saw two static emotional faces on a computer screen and were asked to determine which of the two could have spoken the sentence. The faces had either a strong valence contrast, e.g. a sad sentence followed by a happy face (positive valence) and a sad face (negative valence), or a more subtle, within-valence contrast, such as a sad sentence followed by an angry face and a sad face, both with negative valence. The contrast of two faces with positive valence (happy and positive surprise) resulted in chance level accuracy for all participants and was not included in the final analysis.

Results: A 2 (group) by 2 (prosodic intensity) ANOVA revealed a main effect for intensity (F (1, 42) = 81, $p < .001$), with high intensity prosody resulting in higher accuracy, and an intensity by group interaction (F (1,42) = 5.58, p = .023) showing that the ASD group's accuracy dropped off more sharply than the TD group's for samples with weak prosody. A one-way ANOVA for each condition revealed a significant group difference for samples with weak intensity *and* the more subtle within-valence contrast (p = .007, see Table).

Group accuracy differences based on Oneway ANOVA

	Prosody: Intensity Strong	Prosody:
Face: Negative vs. Positive	No group difference (p=.998)	Trend fo (p=.069)
Face: Negative vs.	No group difference (p=.512)	Sig. grou

Conclusions: Individuals with ASD are as capable as their TD peers at matching sentence-length affective prosody to static facial expressions for basic emotions when prosodic intensity is strong. As prosodic intensity weakens, accuracy drops more sharply in individuals with ASD. When both prosodic intensity and facial expression valence contrast are subtle, adolescents with ASD are significantly less accurate at matching affective voices and faces than their TD peers.

112.89 89 Emotion Recognition in ASD: An Investigation in the Visual and Auditory Modalities. C. R. G. Jones*[1], A. Pickles[2], A. J. S. Marsden[3], F. Happé[4], S. Scott[5], D. A. Sauter[6], J. Tregay[3], R. J. Phillips[3], G. Baird[7], E. Simonoff[8] and T. Charman[1], (1)*Institute of Education, University of London*, (2)*University of Manchester*, (3)*UCL Institute of Child Health*, (4)*Institute of Psychiatry, KCL*, (5)*UCL Insitute of Cognitive Neuroscience*, (6)*Max Planck Institute for Psycholinguistics*, (7)*Guy's Hospital*, (8)*Institute of Psychiatry*

Background:

Autism spectrum disorders (ASD) are characterised by social and communication difficulties in day-to-day life, including problems

in recognising emotions. However, experimental investigations of emotion recognition ability in ASD have been equivocal; hampered by small sample sizes, narrow IQ range and over-focus on the visual modality.

Objectives:

We aimed to assess emotion recognition skills in both the visual and auditory modalities using structural equation modelling (SEM).

Methods:

We tested 89 adolescents (mean age 15;5, mean full-scale IQ 84) with an ASD and 56 adolescents without an ASD (mean age 15;6, mean full-scale IQ 87) on a facial emotion recognition task and two vocal emotion recognition tasks (one verbal with neutral content; one non-verbal). Recognition of happiness, sadness, fear, anger, surprise and disgust was assessed. Using SEM, we modelled the recognition capability for each emotion as a specific latent trait, measured by the three tasks. We examined how the mean levels of the six traits (emotion recognition capability) differed by group (ASD vs. non-ASD) and IQ (>= 80 vs. < 80).

Results:

We did not find any evidence of fundamental difficulties in the recognition of emotion in our ASD group. Further, analysis of error patterns suggested that the ASD group were vulnerable to the same pattern of confusion between emotions as the non-ASD group.

Conclusions:

Using a statistical approach that deals with the problems of multiple testing and a large sample that encompasses the full range of IQ, we do not find evidence that individuals with ASD have a fundamental deficit in the recognition of emotion in the visual and auditory modalities.

112.90 90 Investigating the Role of Emotion Perception in the Communication Skills of Individuals on the Autism Spectrum.

M. S. Banks*[1], D. L. Robins[2], T. Z. King[1] and C. C. Henrich[2], (1)*Psychology, Georgia State University*, (2)*Georgia State University*

Background: Research has shown that children and adolescents with Autism Spectrum Disorders (ASD) have difficulty communicating with others effectively, often to a degree that is unexpected given their level of cognitive functioning. Moreover, emotion perception is widely known to be an area of weakness for these individuals, specifically in identifying emotions of others. Despite the great deal of research investigating both emotion perception and adaptive behaviors such as communication skills, it remains unclear exactly how these two constructs are related with regard to ASD.

Objectives: To assess the relationship between emotion perception abilities and communication skills in children and adolescents on the autism spectrum compared to typically developing individuals (TD). In order to evaluate the mediational hypothesis and account for the non-normality of the sampling distribution, bootstrapping in conjunction with OLS regression was utilized (Preacher & Hayes 2008). Estimates of the indirect effect were obtained with bias-corrected bootstrap confidence intervals.

Methods: 19 children and adolescents with ASD (4 males; mean age = 13.07 years, SD=3.73) and 11 typically-developing controls (2 males; mean age = 12.46 years, SD=3.29) participated as part of a larger study. All subjects were administered the DANVA-2 as a measure of emotion perception ability and completed the four subtests: Adult and Child Paralanguage, Adult and Child Faces. Each subtest consists of 24 faces or voices, with answer choices of happy, sad, angry or fearful. Additionally, the parent/guardian of each participant completed the Vineland Adaptive Behavior Scales – Second Edition (VABS-II) to assess participants' levels of adaptive functioning; the Communication domain score was used in this study. IQ was estimated using the Wechsler Abbreviated Scale of Intelligence.

Results: Individuals with ASD made significantly more errors in emotion perception (M = 16.45, SD=3.80) than did TD individuals (M = 24.95, SD=10.59; F(30)=7.132, p=.003). Additionally, and as expected, the communication skills of individuals with ASD were reported to be significantly lower (SS78.74) than that of TD individuals (SS=103.15; F(30)=.415, p<.001). The total effect of diagnostic group on communication skills was -20.63, SE=5.63, p=.001 when controlling for IQ. The total indirect effect through the mediator, emotion perception ability, has a point estimate of 4.59 and a 95%

Bca bootstrap CI of .8475 to 14.70. That the CI for this indirect effect did not overlap with zero indicates the indirect effect is significantly different from zero at p<.05.

Conclusions: Based on the direction of these results, it appears that, compared to TD individuals, as the emotion perception abilities of ASD individuals decreased (i.e. more errors), their level of communication skills became significantly more impaired. This finding indicates that there may be an important relationship between emotion perception ability and communication skills in individuals with ASD. Further exploration and application of this relationship could facilitate novel emotion perception-focused interventions for advancing the communication skills of individuals on the autism spectrum.

112.91 91 Affective Expression in Verbal Children with Autism during Instrumental and Interpersonal Interactions. K. Leadbitter*[1] and C. Lewis[2], (1)*University of Manchester*, (2)*Lancaster University*

Background:

Kasari et al. (1993) observed that preschoolers with autism were impaired in the timing and use of affective expression. Hobson (1993, 2002) argues that autism involves reduced affective engagement, whilst Mundy (1995) discusses impaired social-emotional approach. The affective expression of school-age, verbal children with autism needs further investigation. There is some suggestion that such children do not differ from comparison groups in affective expression (Capps et al., 1998; Müller & Schuler, 2006). It may be that reduced affect in this subgroup is seen within only certain types of interaction.

Objectives:

To test two hypotheses:

(1) The expression of positive affect will be reduced in verbal children with autism, both during the child communicative acts and communicative partner responses.

(2) This reduced affect will be seen particularly in specific contexts: in 'interpersonal' interactions (those which serve the sole purpose of sharing with another person) rather than in 'instrumental' interactions (those which serve to meet an external goal).

Methods:

Participants: 18 children with ASD and 18 children with learning difficulties aged between 6 and 11 years with language abilities over 3 years. Groups matched on gender, chronological age, and expressive and receptive language. Diagnostic checks completed (ADOS and SCQ).
Procedure: Whilst engaged in the activity of building Lego cars, each child was instructed to deliver a brief message to another adult seated across the room (the communicative partner). Two of these interactions were instrumental (to get the car and to ask where the car was); two were interpersonal (to tell her about the car and to show her the car). After the child delivered each message, the communicative partner responded to the child in a natural positive manner.
Coding: The presence of child positive affect during the child's communicative act and the partner's response was coded from video-tape. Reliability was established on these variables (kappa > .72).

Results:

Overall, children with autism displayed significantly less positive affect. Children with autism expressed affect in 15% of their acts and the children with LD in 21% of acts. The autism group also expressed affect in 15% of responses, compared to 35% of responses for the LD group. The interaction between group and timing of affect approached significance.
However, a significantly greater number of children in the autism group showed affect within their instrumental acts than children in the LD group. Conversely, significantly more children in the LD group expressed affect during the response of the communicative partner in interpersonal conditions.

Conclusions:

Verbal children with autism express less positive affect during brief interactions with an adult. However, this is not across the board. Children with autism more often showed positive affect when communicating to achieve a non-social goal. Children with LD were more likely to smile and laugh in response to a positive and non-instrumental response from an adult. Evidence was found to support the notions of reduced

social-emotional approach and reduced affective engagement. However, a distinction between instrumental and interpersonal contexts is crucial to pinpoint the precise nature of this deficit.

112.92 92 Evidence for a Risk Averse Decision-Making Style in Autism Spectrum Disorders. S. A. Johnson*[1], J. H. Filliter[1], T. J. Pleskac[2], S. Queller[3], A. B. Murton[1], S. E. Bryson[4] and I. M. Smith[4], (1)*Dalhousie University*, (2)*Michigan State University*, (3)*Indiana University*, (4)*Dalhousie University/IWK Health Centre*

Background: Decision-making tasks allow researchers to examine two inter-related processes that are essential to our daily lives: learning and motivation. These tasks assess these processes in the context of non-social stimuli, with reference both to positive and negative outcomes. The Iowa Gambling Task (IGT) has been used to study decision-making in a number of clinical groups, including those with Autism Spectrum Disorder (ASD). Johnson et al. (2006) and Mussey et al. (2008) reported impaired decision-making performance in high functioning individuals with ASD. Given the complexity of the IGT, formal cognitive models have been developed to separate complex behaviour into several component constructs or processes (i.e., new variables) that cannot be derived based on observable behaviour. In our previous study (Johnson et al., 2006) we utilized the Expectancy-Valence Learning model (EVL, Busemeyer et al., 2002) to examine IGT performance and found high attention to loss in the ASD group relative to controls. Additional decision-making tasks, also amenable to formal cognitive modeling, have been used in other clinical groups. Specifically, the Balloon Analog Risk Task (BART, Lejuez et al., 2002) and Game of Dice Task (GDT, Brand et al., 2004) may provide further insight into decision-making processes in ASD.
Objectives: To determine if previously reported differences on decision-making tasks in ASD are task-specific (IGT only) or task-general, we examined the consistency of decision-making results across three tasks.
Methods: Current analyses represent data from 14 youths with ASD (10M/4F) and 16 age- and IQ-matched controls (10M/6F), aged 9-17 years; data collection is ongoing. All participants completed a battery of decision-making tasks including the IGT, BART, and GDT. In addition to traditional group comparisons of task performance, we utilized formal cognitive models to assess IGT and BART performance.
Results: There was a significant difference between groups on the BART ($t(27) = 2.54$, $p = .017$), with the ASD group making fewer risky choices than controls. Mathematical modeling results for the BART indicated group differences on two parameters: 1) the choice consistency parameter, with the ASD group exhibiting more consistent responses than the TD group; and 2) the sensitivity to rewards parameter, with the ASD group showing lower sensitivity to rewards relative to TD participants. Together, these findings suggest that ASD participants were less motivated by reward and demonstrated less exploratory, or risk-averse, response patterns. Consistent with BART findings, the ASD group made fewer risky choices on the GDT than controls, $t(28) = -1.95$, $p = .06$. In contrast to previous findings, there were no group differences on IGT performance, largely because of an unexpectedly flat learning slope for the TD group. There were no group differences on the EVL model of the IGT.
Conclusions: Overall, these findings suggest that children and adolescents with ASD demonstrate a risk-averse decision-making pattern across tasks. Results will be discussed in the context of the preference for sameness and aversion to change often associated with the autism spectrum.

112.93 93 Self-Reported Anxiety Following An Evaluated Verbal Performance Task: Similarities and Differences Between Children with and without Autism. K. Lanni*[1], D. Simon[2] and B. Corbett[2], (1)*Washington State University*, (2)*M.I.N.D. Institute, University of California at Davis*

Background: Autism is a neurodevelopmental disorder characterized by prominent social and communication deficits, as well as increased stress in response to novel situations. The Trier Social Stress Task (TSST) is a standardized social stress protocol that represents a novel social interaction and is known for its ability to reliably induce stress and anxiety, activating the LHPA axis, in a laboratory setting.

Objectives: The current study was designed to investigate the relationship between self-reported trait (persistent) anxiety and self-reported state (present) anxiety following performance of the TSST in children with autism and typically developing children.

Methods: The preliminary study included 25 children ages 8-to-12 years old with autism (AUT, n=11) and with typical development (TYP, n=14).

Participants completed a version of the TSST that has been modified for use with children as well as the State-Trait Anxiety Inventory for Children (STAIC) as part of a larger research protocol. Using analysis of variance, we assessed associations between trait anxiety (persistent), state anxiety (present) and diagnosis across participants.

Results: Self-report of trait (persistent) anxiety varied significantly between the groups [$F(1,24)=10.894$, $p<.01$), such that children with autism report more trait anxiety than typically developing children. However, no significant differences were found between groups for self-report of state (present) anxiety, following completion of the TSST [$F(1,24)=0.234$, n.s.]. As a group, the children with autism reported less state (present) anxiety ($x=32.36$), following TSST performance, than trait (persistent) anxiety ($x=39.36$).

Conclusions: These results provide preliminary evidence for a different pattern of self-reported anxiety in children with and without autism. As expected, children with autism report experiencing higher levels of general anxiety throughout their day than typically developing children. However, following performance of a stress-evoking task, children with autism and typically developing children report comparable levels of acute anxiety. The finding that children with autism report less anxiety following the stressor relative to their general level of anxiety (rather than an increased or stable level) requires further investigation. The limitations of reliance on a self-report measure in children with autism could be one explanation for the above findings (i.e. lack of insight into emotional understanding). Alternatively, it may be the case that children with autism did not perceive the experimental setting or task to be anxiety-provoking; however, this possibility seems unlikely given previous research reporting that children with autism demonstrate increased cortisol following completion of the TSST (Jansen, et al., 2003). To further analyze the present findings, these data will be compared to biological indices of stress, neuropsychological test performance and behavioral ratings of stress as part of a larger study.

112.94 94 Empathy: Understanding and Real Life Behavior in Children with Autism Spectrum Disorder. A. M. Scheeren*, S. Begeer, H. M. Koot and J. van Wijhe, *VU University*

Background: A deviant response to the affective state of others is one of the core features of children with autism spectrum disorders. As they grow older, high-functioning children with autism spectrum disorders (HFASD) develop a relatively adequate insight into emotions and social situations. However, their spontaneous social emotional skills in everyday life remain hampered.

Objectives: In the current study real life empathic skills of children and adolescents with HFASD and typically developing children and adolescents (children: 6-10 years; adolescents: 16-22 years) were assessed and compared to self reported empathic responses.

Methods: All children took part in an individual interview. Practical empathic skills were assessed during standard situations where the interviewer simulated an affective state. Responses of the child were videotaped and coded. Children's self reported empathic behavior was examined by asking them how they would react in comparable hypothetical situations.

Results: Initial analysis revealed no differences between the groups of young children (6-10 years) in number of verbal empathic real life responses to the interviewer. When no verbal response was given, typically developing children paid more attention to the interviewer than the group of children with HFASD. In some cases children with HFASD showed no response at all, this did not happen in the control group. In self reported behavior typically developing children included more empathic responses than children with HFASD.

Conclusions: The results affirm the idea that children with HFASD pay less attention to the affective state of others. At a conceptual level young typically developing children gave more empathic responses than children with HFASD. This difference could be explained by a developmental delay in emotional knowledge of children with HFASD. Children with HFASD could also be less liable to give social desirable answers.

112.95 95 Behavioral and Physiological Responses to Name Call in Young Boys with Autism Spectrum Disorders. M. L. DeRamus*[1], L. Watson[1], G. T. Baranek[1] and J. Roberts[2], (1)*University of North Carolina at Chapel Hill*, (2)*Barnwell College, University of South Carolina*

Background: Evidence demonstrates that children with autism spectrum disorders (ASD) have a

diminished behavioral (head turn) response to name call, but no research indicates whether children with ASD respond physiologically (heart rate) to name call. If a child does not respond to his/her name, the child may miss opportunities for social interaction and learning experiences. Objectives: Determine whether children with ASD present a 1) behavioral and/or 2) physiological response to a name call when compared with language age (LA) and chronological age (CA) matched typically developing (TD) peers. Methods: The current study was a secondary data analysis from a larger grant about language outcomes in 23 boys with ASD (MCA=34.8 m, range 28 to 42 m) and 29 TD boys (MCA= 22.9 m, range 7-42 m) matched for LA (n=15) or CA (n=14). ASD diagnosis was confirmed with the Autism Diagnostic Observation Scale (ADOS), the Autism Diagnostic Interview-Revised (ADI-R), and the Childhood Autism Rating Scale (CARS). Language age was determined by the Preschool Language Scale-Fourth Edition (PLS-4). All participants were given the Mullen Scales of Early Learning, to determine developmental levels in the areas of visual reception, expressive and receptive language, and fine motor skills. In an experimental session, each child watched three minutes of a nonsocial music video while surface electrodes on their chests measured heart rate data. During the third minute, one examiner called the child's name while another examiner activated a switch to insert electronic markers into the heart rate data file. These markers were used to synchronize the name call with the heart rate data. The child's name was presented every 15 seconds for up to one minute (up to 5 trials) until a clear behavioral response, a turn of the head toward the examiner, was observed. Right/left presentation was counterbalanced across children. Videos of the session were coded for head turn response across all trials. Results: Behavioral data indicate 7/23 (30%) children with ASD, 12/13 (92%) of CA children, and 13/15 (87%) of LA children responded with a head turn on the first name call. 5/23 children in ASD group did not respond to name call during any of the 5 trials. All children in TD groups responded to name call. Average number of trials until head turn behavior was 1.27 for LA group, 1.23 for CA group, and 2.17 for 18 responders in ASD group. Analyses of heart rate data are in process. Conclusions: Findings support the literature suggesting children with ASD have a reduced behavioral response to name call. The heart rate data will provide insight into whether children with ASD have a typical physiological response to name call in the absence of a behavioral response.

112.97 97 Face Scanning Distinguishes Social and Communication Impairments in Autism. T. Falck-Ytter* and C. von Hofsten, *Uppsala University*

Background: How closely related are the social and communicative impairments in Autism Spectrum Disorder (ASD)? Recent findings in typically developing children suggest that both are highly heritable but have only moderate behavioural and genetic overlap. The face transmits both socio-emotional and communicative information. Fixating the eyes is important to detect certain emotions such as fear, while fixating the mouth facilitates language comprehension.

Objectives: The present eye tracking study aimed at testing the hypothesis that social impairment symptoms and communication problems are differentially related to face scanning in ASD. Specifically, we expected children better at socio-emotional behaviors to fixate the eyes more than the mouth, while the opposite was expected for children better at communication.

Methods: The gaze of 15 young children with formal DSM-IV diagnosis within the Autism Spectrum and a typically developing group was recorded with an eye tracker (Tobii 1750) while they looked at several male and female faces. We related the Social Impairment scale and the Communication Impairment scale of the Autism Diagnostic Interview –Revised (ADI-R) to where in the face they were looking (eyes or mouth).

Results: We show that when looking at other people's faces, children with ASD who are better at social interaction than communication look more at the eyes, while the children better at communication than social interaction look more at the mouth.

Conclusions: This study suggests that the neural systems for social-emotional and communication behaviors are clearly separable in ASD, and that in face observation, they give opposing instructions to the oculomotor system. We believe this finding has important theoretical and clinical implications.

112.98 98 Identification of Distinctive Faces in Individuals with Autism. D. Wilkinson*[1], N. J. Minshew[2] and M. S. Strauss[1],

(1)*University of Pittsburgh*, (2)*University of Pittsburgh School of Medicine*

Background: Research indicates that typically developing children as young as 4 years of age discriminate distinctive faces from average looking faces. (McKone & Boyer, 2006). Additional research with both children and adults has shown that distinctive faces are remembered better than less distinctive faces (i.e., the distinctiveness effect). The distinctiveness effect is frequently explained using Valentine's theoretical multidimensional face space (1991). In this model, typical or average faces, which are more prototypical, are stored at the center of the face space. In contrast, distinctive faces which deviate more from the prototypical face are stored toward the perimeter of the face space. Since the majority of faces are stored near the center of the face space, distinctive faces are easier to recall. Preliminary evidence suggests that face recognition in children and adults with autism is not aided by distinctiveness. However, it is unclear whether individuals with autism are unable to identify distinctive faces or whether distinctive faces simply do not enhance their memory recall.

Objectives: The current study examined adults with autism's ability to identify distinctive faces in order to expand on research which indicates that individuals with autism do not demonstrate a distinctiveness effect. Thus, this study explored whether individuals with autism are able to choose the more distinctive face. In addition, this study manipulated the difficulty of the task to determine the degree to which individuals with autism have an understanding of face distinctiveness.

Methods: Participants included high-functioning adults with autism who ranged in age from 18 years to 42 years of age. Control participants included adults without autism matched on age and gender. The study consisted of 30 trials, in which participants were asked to choose which of two faces was more distinctive. Facial stimuli consisted of 60 female faces that had been rated by a separate sample of adults without autism on distinctiveness using a 7-point scale. Trials were divided into three difficulty groups based on the magnitude of the change in distinctiveness between the two faces: hard, moderate, and easy.

Results: Preliminary analysis indicated that overall, individuals with autism were less accurate at identifying the more distinctive face compared to control individuals. Furthermore, while adults in the control group performed better than chance on both the easy and the moderate difficulty trials, adults in the autism group performed better than chance only on the easy trials. As expected, accuracy for both groups decreased as trial difficulty increased.

Conclusions: These results indicate that adults with autism are impaired in their ability to identify distinctive faces. While individuals with autism were able to identify distinctive faces on the easy trials, they were not able to on more difficult trials. Thus, the lack of a distinctiveness effect in individuals with autism may arise from a failure to discriminate between distinctive and typical faces. More generally, these results suggest that individuals with autism are not learning and storing faces in an organized "face space" as do typically developing individuals.

112.99 99 Fixation Patterns to Faces in Autism: Investigating the Influence of Task Requirements. D. P. Kennedy*, J. Gläscher, M. L. Spezio, L. K. Paul and R. Adolphs, *Caltech*

Background: Although reduced eye contact in autism is a clinically and anecdotally well-established phenomenon, experimental studies aimed at quantifying this phenomenon have yielded mixed results. In part, this may be explained by differences in the type of face stimuli used [for example, static vs. dynamic faces (Speer et al., Autism, 2007) and intact vs. degraded faces (Spezio et al., JADD, 2007)]. However, it remains unclear as to whether inconsistent findings might also be explained by differences in task demands rather than just the nature of the stimuli.

Objectives: Here we provide a detailed characterization of the role of task demands on scan patterns to faces in autism, as well as comparisons with control participants. By using identical face stimuli across a series of different tasks, and running each task on each participant, we determine the contributions of, and interactions between, task requirement and participant on scan patterns to faces.

Methods: While undergoing eye-tracking, subjects viewed smiling direct-gaze male and female face images while performing the following tasks, presented in a random order: (a) passive viewing,

(b) gender discrimination, (c) 2-back gender discrimination, and (d) friendliness judgment. Images were presented to the subject in a gaze-contingent manner wherein subjects had to first fixate on a cross on one side of the screen before the image would appear on the opposite side of the screen. Analyses of interest include location and latency of first fixations, number of fixations, and the amount of time fixating various features of the face (e.g., eyes, mouth).

Results: Preliminary analyses of 5 adult participants with autism and 6 neurotypical control participants confirm that individuals with autism spend less time fixating the eye region of faces, relative to controls. Furthermore, across the various tasks, fixation patterns are remarkably consistent within an individual participant. However, there are differences across participants, with some participants consistently making more or less eye contact than other participants.

Conclusions: Thus far, results suggest that task requirements have little influence on how individuals with autism fixate faces. Rather, differences in scan patterns are seen between individuals. If these findings were confirmed in a larger group, this would suggest that the inconsistencies in the literature regarding reduced eye contact in autism are likely driven in large part by differences in the study participants, and possibly also differences in the type of stimuli used, rather than differences in task requirements. Data collection is ongoing, and the results from a larger group of participants will be reported.

112.100 100 The Impact of Perceptual and Social Mechanisms on Human vs. Cartoon Emotion Processing in Children with High-Functioning Autism. D. Rosset*[1], D. Da Fonseca[1], A. Santos[2], F. Poinso[3] and C. Deruelle[2], (1)*INCM, CNRS; Autism Resource Center*, (2)*INCM, CNRS*, (3)*Autism Resource Center*

Background:

Atypical facial emotion processing is one of the main features of autism spectrum disorders. Interestingly, recent evidences suggest that this might be specific to the processing of facial expressions displayed in human faces and might be spared in cartoon face processing. However, to date, the reasons why children with autism process emotions in human and cartoon faces differently remain unclear.

Objectives:

The aim of the present study was to examine the influence of perceptual and social mechanisms on the processing of human vs. cartoon faces in children with high-functioning autism (HFA).

Methods:

This study included 20 children with HFA matched to 20 typically developing controls. Stimuli comprised digitized faces morphed (20% signal increment) to produce a linear continuum of images between the two endpoints (cartoon and human faces). These faces were presented either upright or inverted in order to assess the perceptual strategy used in face processing. Children were first asked to judge the emotion displayed on the faces (session 1) and then asked to categorize the faces into categories – cartoon or human faces (session 2).

Results:

In the first session, a significant inversion effect was found for both HFA and control groups, independently of the morphed face. In the second session, both groups showed a similar categorical boundary, although performance at the endpoints was lower for the HFA than the control group. Importantly, this group difference was found for human faces but not for cartoon faces.

Conclusions:

Findings of this study revealed that both children with HFA and controls used similar perceptual strategies to recognize emotions on human and cartoon faces. In addition, and in line with results for controls, children with HFA were found to rely on the same perceptual criteria to categorize human and cartoon faces. These findings suggest that perceptual mechanisms do not underlie atypical human vs. cartoon face processing in children with HFA. By contrast, poor performance of children with HFA relative to controls on the categorization of human faces suggest a top-down influence of social mechanisms on facial emotion processing in children with HFA. These findings are in agreement with clinical and parental reports of great interest for cartoon characters relative to reduced interest for human faces in children with autism.

112.101 101 Can People with Asperger Syndrome Identify Fake Smiles?. S. J. Wheelwright*, C. Dickinson, V. Pile, A. Seleznev and S. Baron-Cohen, *University of Cambridge*

Background: Although adults with Asperger Syndrome (AS) are usually not impaired at identifying happy faces, one previous study indicates that AS adults find it difficult to identify fake smiles (Boraston *et. al.*, 2008). In both genuine ("Duchenne") and fake smiles, the zygomatic major muscle contracts, pulling up the corners of the lips. However, in genuine smiles there is also contraction of the external orbicularis oculi muscle, causing "crow's feet" to appear on the outer sides of the eyes, the cheeks to raise and the eye aperture to narrow. Whether people with AS can distinguish real vs. fake smiles is important because of its relevance to social skills, and because this could reflect a specific instance of impairment in empathy (emotion recognition and attribution of intent). However, in the Boraston study, stimuli comprised just ten repeated female faces, and smile intensity in the mouth region differed between the real and fake smiles. There is therefore a need to test if this finding replicates, using improved stimuli.

Objectives: To replicate the finding that AS adults are impaired at identifying fake smiles with improved stimuli.

Methods: 15 males with AS and 20 control males aged 18-40 years, matched for IQ, participated. In Task 1, participants had to indicate whether they thought a smile was real or fake using a simple button box. Stimuli consisted of 92 photographs of smiling real faces, half of which were genuine smiles and half were fake smiles, each presented for 2955ms in a random order. The fake smiles were created by merging the mouth region from the genuine smile with a neutral expression. There were 25 female actors and 21 male actors who each appeared twice, once with a genuine smile and once with a fake smile. In Task 2, the 46 pairs of smiles were presented side by side and participants had to indicate which of the pair was the genuine smile. Accuracy and reaction times (RTs) were recorded.

Results: On Task 1, the AS group correctly identified 72% of the real smiles but just 49% of the fake smiles. In the control group, the figures were 78% and 63% respectively. Analysis showed that both groups were more accurate with real smiles and that, overall, controls were more accurate than the AS group. Both groups were faster on the real smiles and there was no group difference in RTs. Controls were better than the AS group at judging which smile was fake when the faces were presented in pairs (92% vs. 83%). The group difference for RT approached significance, with the control group being faster than the AS group. Actor sex had no effect throughout.

Conclusions: Participants with and without AS find it difficult to identify fake smiles. Presenting a fake and real smile simultaneously improves performance in both groups, but the AS group is still measurably less accurate than the control group. Because it is challenging, the Fake Smile Test could be used as a subtle test of empathy.

112.102 102 Do You See What I See? the Influence of Working Memory on Shared Knowledge in Children with Autism and Typical Development. J. Schuh*, D. Mirman, T. Gustafson and I. M. Eigsti, *University of Connecticut*

Background:

Pragmatic impairments in autism spectrum disorders (ASD) are significant, and are uniquely impaired as children with ASD mature (e.g., Paul et al., 2005). Impairments in executive function, or the allocation of attentional and cognitive resources, may influence pragmatic language ability; specifically, working memory (WM), involved in updating and maintaining representations, may play a central role. This study explores pragmatic language and WM interactions by assessing whether children with ASD maintain accurate representations of what knowledge is shared between conversational partners. This skill, known as *common ground* (Clark, 1992), has not been previously explored in ASD. The current study utilized a cooperative problem-solving task in which a participant places shapes onto a visual display according to a confederate partner's spoken instructions; some shapes are unknown to the partner. Previous studies of typical development suggest that while participants' ultimate *responses* indicate their knowledge of what shapes are unknown, and thus unlikely to be referred to by the partner, their *eye-movements* indicate significant competition from these "secret" shapes. Increasing the number of secret shapes provides a manipulation of WM demands. Examining both overt responses and eye movement patterns allows us to examine

the interactions among pragmatic language and WM skills in ASD.

Objectives:

The primary goals were to 1) examine the role of WM in a CG task, and 2) explore group differences between children of TD and with ASD, to determine the influence of WM load on perspective-taking during discourse. If WM abilities are critical in maintaining CG, then they may account for some of the variation in pragmatic impairments observed in ASD.

Methods:

Children with ASD (mean age, 11.8 years) and age- and IQ-matched typically developing controls (n = 4 per group) cooperated with a partner (a trained research assistant) to solve a puzzle, following the partner's instructions to move shapes onto a grid presented on a computer. Participants' eye movements were tracked during the task. The number of secret shapes, known only to the participant, was manipulated to assess the role of WM. Final analyses will be reported for 40 children (ASD n=20) ranging from 9 to 16 years old.

Results:

Preliminary data indicated that all participants were accurate in their behavioral responses (81%). Eye-movement data indicated that all participants looked more closely, p<0.001, and fixated more quickly, p<0.01, to the target shape. However, the ASD group fixated less accurately, p<.01, and appeared to disambiguate the target more slowly, p<.001, than controls. In addition, differences in performance for low versus high WM conditions suggested that the ASD group was more susceptible to WM demands in this task, consistent with predictions. Overall, eye fixation patterns suggested that children with ASD had greater difficulty differentiating between target and secret shapes.

Conclusions:

Results are consistent with previous studies suggesting taking another's perspective requires additional processing capacity. Examining the processes underlying pragmatic deficits, such as WM and common ground, will allow for a better understanding of the deficits, and can also illuminate the role of WM in the symptomatology of ASD.

112.103 103 Do Others' Faces Hold Attention in Children with ASD When They Fixate to the Eyes?. Y. Kikuchi*[1], A. Senju[2], H. Akechi[1], Y. Tojo[3], T. Hasegawa[1] and H. Osanai[4], (1)*The University of Tokyo*, (2)*Birkbeck, University of London*, (3)*Ibaraki University*, (4)*Musashino Higashi Gakuen*

Background: Others' faces hold attention longer than non-facial objects in typically developed individuals (Bindemann et al., 2005). In our previous study, we demonstrated that faces hold attention longer than non-facial objects in typically developing children. In contrast, children with ASD did not show such specifically longer attentional dwelling towards others' faces (IMFAR 2008). It is reported that individuals with ASD look at eyes less than typically developed individuals (Klin et al., 2002; Pelphrey et al., 2002). Moreover, individuals with ASD reportedly show comparable level of activation in fusiform gyrus as typically developed individuals when they were instructed to fixate to the eyes of the facial stimuli (Hadjikhani et al., 2004, 2007) and the amount of fixation to the eyes of the facial stimuli correlated with the activation of the fusiform gyrus in individuals with ASD (Dalton et al., 2005).

Objectives: Using the gap and overlap paradigm, we investigated the attentional disengagement from faces and non-facial objects in children with and without ASD when they were instructed to fixate to the eyes.

Methods: Participants consisted of 11 children with ASD (mean 13.2 years; range 10-16 years) and 11 typically developing children (mean 12.3 years; range 10-14 years) matched on IQ. Children were required to saccade towards a peripheral target that followed the central fixation, and children's eye movements were recorded using electrooculography (EOG). In the gap condition, a central fixation face or object disappeared 200 ms before onset of the peripheral target. In the overlap condition, the central fixation face or object remained until the children's response. In order to assure that the participants fixate to the eyes, a fixation cross was presented in the middle of the eyes, and participants were instructed to fixate to the cross and detect the gaze shifts, which occurred occasionally between the test trials. In the object condition, a fixation cross and a bar were also presented and participants were instructed to detect when the bar changed to an arrow, which also occurred occasionally between the test trials. The experimental design consisted of one between-participants factor of Group (children with ASD or typically developing children) and two within-participants factors of Synchronization (gap or overlap) and Stimulus (face or object).

Results: Only the interaction between Synchronization and Stimulus was significant. In the gap condition, SRT was not different between the face and object condition. In the overlap condition, SRT for faces was longer than that for objects. No other interactions, including any effects of Group, were significant.

Conclusions: When participants were instructed to fixate to the eyes, faces hold attention longer than objects, and no group difference was found on this effect.

112.104 104 Do Children with ASD Use Referential Gaze to Learn the Name of An Object?: An Eye-Tracking Study. H. Akechi*[1], A. Senju[2], Y. Kikuchi[1], Y. Tojo[3], H. Osanai[4] and T. Hasegawa[1], (1)*The University of Tokyo*, (2)*Birkbeck, University of London*, (3)*Ibaraki University*, (4)*Musashino Higashi Gakuen*

Background: Some studies reported that children with autism spectrum disorder (ASD) do not refer to other's gaze when they learn novel word-object association (e.g. Baron-Cohen et al., 1997). However, it is not clear whether it is due to the difficulty in following speaker's gaze, or the difficulty in encoding the referential nature of the gaze.

Objectives: To investigate the relationship between gaze following and the use of referential gaze in the learning of novel word-object association in children with ASD, by measuring their fixations with eye-tracking device.

Methods: Participants consisted of 16 children with ASD (mean age 9.2; range 6-11) and 16 typically developing (TD) children (mean age 8.7; range 6-11), who were matched on VMA. The schematic face (speaker) and two novel objects were presented on the monitor. When the participant looked at one of the objects for 300 ms, the speaker uttered a novel word (e.g. toma) and simultaneously shifted his gaze either to the object being looked at by the participant (congruent condition) or the other object (incongruent condition), which was repeated twice. After that, 4 novel objects (2 previously presented and 2 new) were presented and the speaker asked participants "which one is xxx (e.g. toma)?", and their manual responses (i.e. pointing to one of the objects) and fixations were recorded.

Results: Total looking time to speaker's face did not differ between groups. In the congruent condition, equal numbers of children in each group (13) chose the object being looked at by the speaker. In incongruent condition, in contrast, fewer children with ASD (10) than TD children (15) chose the object being looked at by the speaker. In addition, children with ASD who chose the correct object followed speaker's gaze more than those who failed to choose the correct object.

Conclusions: Results suggest that children with ASD, on average, have difficulty in using referential gaze of the speaker to learn the name of a novel object, which may be related to the reduced spontaneous gaze following.

112.105 105 Combining Computerized Cognitive Measures to Improve the Classification of Autism. J. Breidbord*[1], B. Chakrabarti[2], S. J. Wheelwright[1] and S. Baron-Cohen[1], (1)*University of Cambridge*, (2)*University of Cambridge, Autism Research Centre*

Background: Cognitive tests in computerized format offer precise administration, convenient online presentation, and comprehensive assessment in research or clinical practice. These applications present new opportunities to examine behavioural features and indicators of autism spectrum conditions (ASC), useful for sensitive endophenotype identification and better subclassification.

Objectives: To develop a composite index, optimized for identification of adults with a clinical ASC diagnosis, using computerized measures of cognition.

Methods: Adults with (n=232) or without (n=351) a clinical ASC diagnosis completed the Autism-Spectrum Quotient (AQ) and performance measures of empathy (Reading the Mind in the Eyes Test, RMET; Karolinska Directed Emotional Faces Test, KDEFT), visuospatial ability (Embedded Figures Test, EFT; Mental Rotations Test, MRT), and nonverbal intelligence (Raven Progressive Matrices). Composite indices, each optimized for 35% or less false prediction, were formed by systematic combination of the computerized tasks administered online. Candidate classifiers were compared in terms of performance (e.g., sensitivity, accuracy) and predictive power (i.e., incremental value).

Results: Composite indices showed improved overall accuracy (max 80%) when compared to constituent tasks (max 64%). Receiver-operating characteristics identified best performance of the [RMET+KDEFT+EFT] index for general classification of adults with or without a clinical

ASC diagnosis. With respect to subclassification, the [RMET+KDEFT+EFT+MRT] index best differentiated between adults with a clinical ASC diagnosis in the presence or absence of other psychiatric conditions.

Conclusions: Composite indices of cognition designed for specific autism classification performed better than constituent tasks. This use of multidimensional behavioural data supports future efforts to identify other markers of ASC, which could be incorporated into a further-improved index.

112.106 106 The Paradox of Cognitive Flexibility in Autism. H. M. Geurts*[1], B. Corbett[2] and M. Solomon[3], (1)*University of Amsterdam*, (2)*M.I.N.D. Institute, University of California at Davis*, (3)*MIND Institute, Imaging Research Center*

Background: Researchers and clinicians assume that inflexible everyday behaviors in autism are directly related to cognitive flexibility deficits as assessed by clinical and experimental measures. However, there is a large gap between the day-to-day behavioral flexibility and that measured with so called cognitive flexibility tasks.

Objectives: We question the belief that cognitive flexibility is pathognomonic to autism. We will address why this is important, why cognitive flexibility deficits are considered central to autism spectrum disorder, and why we are skeptical.

Methods: We present an overview of current literature addressing cognitive flexibility in autism spectrum disorders.

Results: Based on recent studies at multiple sites, using diverse methods, and participants of different autism subtypes, ages, and cognitive levels, no consistent evidence for cognitive flexibility deficits was found.

Conclusions: To advance the field, experimental measures must evolve to reflect mechanistic models of flexibility deficits. Moreover, ecologically valid measures are required to be able to resolve the paradox between cognitive and behavioral inflexibility.

112.107 107 Evidence for Thinking in Pictures as a Cognitive Account of Autism. M. Kunda* and A. K. Goel, *Georgia Institute of Technology*

Background:

Many theories have been proposed that seek to explain autism at the cognitive level, such as Mindblindness, Weak Central Coherence, and Executive Dysfunction, although no consensus has yet been reached, and even the idea that a single cognitive explanation can be found has been called into question. One view of cognition in autism that has not, however, been investigated in a comprehensive manner in the scientific literature is that of a bias towards "visual thinking" in autism, as exemplified by Temple Grandin's autobiographical book "Thinking in Pictures" and other introspective accounts.

Objectives:

To develop a well-defined hypothesis of cognition in autism centered around a reliance on pictorial representations versus verbal representations. Also, to evaluate this hypothesis with respect to existing empirical data and to examine the relationships between this hypothesis and existing cognitive theories of autism.

Methods:

First, a set of minimal definitions was developed to distinguish between pictorial and verbal representations in terms of their computational properties and to formulate a "Thinking in Pictures" hypothesis of cognition in autism. Then, existing empirical data from relevant published studies in the areas of behavior, cognition, and neurobiology were evaluated in light of this hypothesis, as were data typically cited in support of three existing cognitive theories--Mindblindness, Weak Central Coherence, and Executive Dysfunction.

Results:

Behavioral predictions made from the Thinking in Pictures hypothesis are consistent with many of the atypical behavioral characteristics of autism. Empirical evidence that is relevant to the Thinking in Pictures hypothesis includes cognitive studies of individuals with autism showing a bias towards pictorial versus verbal representations while performing different activities, such as serial recall, task-switching, and semantic retrieval, although contrasting studies suggest that such a bias may not be uniform across the population. Many individuals with autism have often demonstrated intact or even enhanced visual reasoning skills relative to the typically developing

population, such as on the Embedded Figures Task and other visual search tasks as well as on visual tests of reasoning, such as Raven's Progressive Matrices. Also, neuroimaging studies of individuals with autism performing certain tasks have shown greater brain activation in posterior sensory processing and imagery areas in comparison to the typically developing population, who show activation in verbal and other more frontal regions for the same tasks.

Conclusions:

This "Thinking in Pictures" account of cognition in autism shows significant potential for explaining many behaviors and cognitive characteristics in autism. However, open questions remain as to whether only a specific subset of behaviors might be explained by this hypothesis and whether this hypothesis might apply to only a specific subset of individuals with autism. With additional research, this hypothesis may lead to new and innovative methods of communication with and education of individuals on the autism spectrum.

112.108 108 Autism Severity and Its Impact on Cognitive Development in Young Children with Autism. G. Mathai*[1], L. Sears[1] and L. A. Ruble[2], (1)*University of Louisville*, (2)*University of Kentucky*

Background: Autism is a complex neurobiological disorder. Its core deficits of communication, social interaction and restricted/repetitive behaviors have a tremendous impact on how individuals function and cope with various demands over the life span. Key social communication deficits in children with ASD are in the areas of joint attention (coordinating attention from object to person), reciprocal interactions such as giving, taking turns and sharing (Kasari, Freeman & Paparella, 2006). Motor and sensory repetitive behaviors (RSBs) have been associated more with younger ages (Militerni et al., 2002), its impact on cognitive abilities needs further investigation.

Objectives: The purpose of this study is to examine how social communication deficits and RSBs impact cognitive development in young children with autism. The information thus obtained would be critical to determining specific areas for intensive early intervention.

Methods: This analysis was conducted on 56 children diagnosed with Autism based on DSM IV criteria. The sample included children ranging from 2.5 years to 6.0 years. Of these participants, 47 were males and 9 were females. Cognitive functioning was assessed using the 4 core subtests of the lower preschool level of the Differential Ability Scales (DAS). The Preschool level is usually for ages 2:6 to 3:5, but complete norms are available up to age 6:11, which allows for lower-ability 6-year-olds to be tested at a more appropriate developmental level. The 4 core subtests comprise of Block Building (visual-perceptual matching), Naming Vocabulary (expressive vocabulary), Verbal Comprehension (receptive language) and Picture Similarities (non verbal reasoning). Autism severity was assessed using the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 1999; Lord et al., 2000). Module 1 or 2 was used depending on individual child's expressive language abilities. The ADOS variables of interest were total scores for communication (directing facial expressions, vocalizations to others, conversation), reciprocal social interaction (eye contact, initiating and responding to joint attention, shared enjoyment), Play (functional and imaginative play) and Stereotyped behaviors /Restricted Interests (unusual sensory interests, repetitive interests, complex mannerisms).

Results: Multiple regression analysis was used to determine, from five predictor variables (severity of symptoms as measured by the ADOS) those that would be most predictive of the dependent variable (DAS subtest). Four separate analyses were conducted using forward method of entry (with criteria of $p < .05$ to enter variables) on each of the four core DAS subtests. Correlations showed that ADOS social interaction was significantly ($p < .05$) related to DAS block building ability scores. ADOS socialization and communication scores was significantly ($p < .05$) related to DAS Naming ability scores. ADOS stereotypical behavior scores was significantly ($p < .05$) related to DAS Picture Similarities ability scores. ADOS play score was significantly ($p < .05$) related to DAS Verbal Comprehension ability scores.

Conclusions:

Results clearly demonstrate that core deficits in autism impact cognitive development in the areas of imitation, visual perceptual matching, non verbal reasoning and receptive expressive language skills. Interventions in young children

with autism need to focus on preverbal/verbal language skills, play and social interactional skills.

112.109 109 Autism Spectrum and Executive Function. R. Pytlik*, F. R. Ferraro and N. Seibold, *University of North Dakota*

Background: **We examined the relationship between high functioning Autism Spectrum disorder (HFA), as measured by the Autism Spectrum Quotient (ASQ) questionnaire, and underlying neuropsychological performance, specifically frontal lobe and executive function, as measured by the Executive Function Index (EFI, Spinella, 2004). There is some indication that deficits in executive function are a hallmark of HFA (Joseph, et al., 2005) and that HFA individuals lack certain aspects of motivation (Charman, 2005), which also relates to frontal lobe function.**

Objectives: **To date, no one has used the ASQ and EFI together in a single study. We expect greater executive function deficit (lower EFI scores) in individuals possessing a greater number of HFA traits and behaviors (higher ASQ scores), as compared to individuals as possessing fewer such traits and behaviors. Thus, the association between ASQ scores and EFI scores should be negative.**

Methods: **Fifty-five undergraduates took the Autism Spectrum Quotient (ASQ) and the Executive Function Index (EFI). Hurst, et al. (2007) have recently showed that the AQ shows good validity, test-retest reliability, and internal consistency. The ASQ can rapidly (it contains 50 questions, 10 each in 5 domains including social skill, attention switching, attention to detail, communication, and imagination) quantify where an individual falls on the continuum from autism to normality, with scores at or above 32 useful for distinguishing between individuals who have clinically significant levels of autistic traits and those that do not. Subjects also took the Executive Function Index (EFI; Spinella, 2004), a 27 item self-report scale that measures five areas associated with frontal lobe function (motivational drive, strategic planning, organization, impulse control, empathy, plus a total score). Higher scores indicate better frontal lobe functioning.**

Results: **ASQ scores ranged from 5-28 (Mean = 13.85, SD = 5.11). Across the 5 EFI domains, scores ranged from 11-30, with total score ranging from 87-126 (mean = 104.96). Pearson correlations between ASQ and EFI scores resulted in the following: Motivational Drive (r = - .20, p = .07), Impulse Control (r = .07, p = .31), Empathy (r = -.10, p = .24), Organization (r = - .11, p = .22), Strategic Planning (r = .11, p = .21), EFI Total (r = -.06, p = .33).**

Conclusions: **Many of the associations we predicted (as ASQ increases, EFI decreases) were in the right direction. Increases in ASQ score (suggesting more HFA behaviors), resulted in decreases in EFI scores, suggesting more executive function deficit (for Motivational Drive, Empathy, Organization, and EFI Total). Charman (2005) showed that HFA individuals show evidence of a lack of motivation regarding sharing intentions and the correlation between ASQ and**

Motivational Drive
was r = - .22, p = .07. It should be noted that none of the 55 subjects tested thus far have exceeded the cut-off score of 32, which may also have impacted results. Regardless, the EFI is a quick, reliable, and valid indicator of various domains of executive function and may be a useful tool for those investigating frontal lobe deficit and its impact on HFA individuals.

112.110 110 Imagination, False Belief and Counterfactual Reasoning in Children with Autism Spectrum Disorders. S. Begeer*[1], M. Meerum Terwogt[2], P. Lunenburg[3] and H. Stegge[2], (1)*VU University*, (2)*VU University Amsterdam*, (3)*De Bascule*

Background:
Poor imaginative abilities are a central feature of children with high functioning autism spectrum disorders (HFASD). Imagination has been linked to key aspects of cognitive development such as false belief reasoning (reasoning about beliefs that are false) and counterfactual reasoning (reasoning about events that are false). However, few studies have looked at the functional use of imagination in these domains of cognitive development in HFASD. The current study focused on the development of imagination and its use in counterfactual and false belief reasoning of children with high functioning HFASD.
Objectives:

To investigate the development of the use of imagination in additive ('If only I had done…') and subtractive ('If only I had not done….') counterfactuals and false belief reasoning of children with HFASD and typically developing controls, aged 6 to 12 years (n=147), using a cross sectional design of three age cohorts.
Methods:
Children with HFASD (n=76) and typical development (n=71), matched on mental and chronological age, were divided equally over age cohorts of 6-8, 8-10 and 10-12 year olds. Children were presented four stories where they could generate additive and subtractive counterfactuals based on a given consequent (e.g., 'you play in the mud, and then leave muddy footprints all over the kitchen. How could that event have been prevented?'). Furthermore, generative imaginative ability was investigated using an ideational fluency task, and false belief reasoning was tested with a second order false belief task.
Results:
The HFASD group performed more poorly than controls on the false belief and ideational fluency tasks, but not on the counterfactual task. However, a Group*Age*Direction interaction suggested distinct developmental patterns in HFASD and controls. Children with HFASD increasingly used subtractive counterfactuals as they got older. In contrast, typically developing controls showed an increase in additive counterfactuals. Moreover, false belief reasoning was correlated to subtractive counterfactual reasoning in the HFASD group, and to additive counterfactual reasoning in the control groups.
Conclusions:
The opposite developmental patterns of additive and subtractive counterfactual reasoning in children with HFASD and typical development suggest contrasting learning effects. The increase in additive counterfactual reasoning of typically developing children may be linked to their growing adaptive and flexible skills, both cognitive and behavioural. Children with HFASD likely develop different strategies, as evidenced by the link between subtractive counterfactual abilities and false belief reasoning. The role of IQ and ideational fluency will be discussed.

112.111 111 Executive Functioning in Young Adults with Sub-Threshold Autism Traits. S. E. Christ*[1], S. M. Kanne[1] and A. Reiersen[2], (1)*University of Missouri*, (2)*Washington University at St. Louis Missouri*

Background: Recent research (Jobe et al, 2007; Kanne et al., in press) has documented increased psychosocial difficulties in individuals who report higher-than-typical autistic traits but without an Autism Spectrum Disorder (ASD) diagnosis. Little is known, however, regarding the cognitive profile of this broader autism phenotype.

Objectives: To explore whether individuals who report sub-threshold autistic traits also report cognitive difficulties that are similar to those experienced by individuals with ASD.

Methods: A screening version of the Social Responsiveness Scale (SRS) was administered to over 1800 young adults and used to identify 35 individuals (ages 18-21) reporting greater social difficulties (High Trait Group). Seventy-one individuals reporting minimal difficulties were also identified (Low Trait Group). Group differences in autistic traits were further confirmed using the Autism Spectrum Quotient, $t(104) = 11.0$, $p < .001$. The groups were matched based on the extent of reported ADHD symptomatology, $t(104) < 1$, $p > .05$. For the present study, we utilized the Behavior Rating Inventory of Executive Function (BRIEF) to evaluate behavioral aspects of executive functioning in both groups.

Results: Overall, individuals in the High Trait Group [mean Global Executive Composite (GEC) = 64.5] reported greater executive difficulties than individuals in the Low Trait Group [mean GEC = 56.2], $t(104) = 4.2$, $p < .001$. Significant group differences (High Trait Group > Low Trait Group) were also found on all BRIEF subscales (e.g., Shift, Initiation, Working Memory, Plan/Organize) and remaining index scores (e.g., Behavior Regulation Index), with the exception of the Inhibit subscale and Organization of Materials subscale, $p > .05$ in both instances.

Conclusions: Consistent with prior literature documenting executive function impairment in individuals with ASD, we found that individuals with a higher degree of autistic traits (but no ASD diagnosis) reported greater levels of executive difficulty as compared to typical control individuals. Interestingly, the low and high trait groups did not differ on the inhibitory control scale, an area of functioning that appears to be largely spared in individuals with ASD as well (for exception, see Christ et al., 2007).

112.112 112 Executive Functioning in Children with ASDs Who Have Achieved Optimal Outcomes. E. Troyb*, M. Rosenthal, K.

Tyson, M. Helt, I. M. Eigsti, L. Naigles, M. Barton and D. Fein, *University of Connecticut*

Background: Since Lovaas (1987) first reported that children with Autism Spectrum Disorders (ASD) can achieve favorable outcomes following early intensive, behavioral intervention, few studies have investigated "recovery" from ASD. In addition, research examining the residual impairments in cognitive functioning of children with ASD who achieve optimal outcomes has been scarce.

Objectives: This study examines the executive functioning of a small group of children who received an ASD diagnosis before age 5, but no longer meet criteria for an ASD diagnosis at the time of testing. This study refers to this group as optimal outcome children.

Methods: Nineteen children with optimal outcomes (OO, M(age) =12.6), have been matched on their age, sex, Full Scale IQ, Verbal IQ and Nonverbal IQ, with 13 high functioning children with a current ASD diagnosis (HFA, M(age) = 13.1), and 23 typically-developing peers (TD, M(age) = 13.4). The groups were compared on performance on the D-KEFS Tower of London, Color-Word Interference and Verbal Fluency subtests. In addition, 10 of the 19 OO children were also compared to nine HFA children and 22 TD peers, on parental responses on the Behavior Rating Inventory of Executive Function (BRIEF).

Results: Performance on the subtests of the D-KEFS did not differ significantly between the three groups and all were within the average range. On the BRIEF, OO children performed in the average range on all subscales. They showed less impairment than HFA children in working memory (M(OO)=53.0, M(HFA)=64.4, p=.02), as well as in their ability to shift easily between activities (M(OO)=50.9, M(HFA)=72.6, p<.01), regulate emotional reactions (M(OO)=47.3, M(HFA)=63.2, p <.01) and self-monitor (M(OO)=51.3, M(HFA)=65.8, p<.01). However, OO children had more difficulty than their TD peers in their abilities to inhibit impulses (M(OO)=53.9, M(TD)=44.0, p=.02), shift easily between activities (M(OO)=50.9, M(TD)=41.9, p=.02), regulate emotional reactions (M(OO)=47.3, M(TD)=41.4, p=.03), initiate activities (M(OO)=53.2, M(TD)=41.8, p=.02) and self-monitor (M(OO)=51.3, M(TD)=43.5, p=.04). They also showed greater impairments than TD peers in working memory (M(OO)=53.0, M(TD)=42.9, p=.01), planning and organization (M(OO)=52.8, M(TD)=44.1, p=.02). These differences, however, were due to the superior performance of the TD group.

Conclusions: Preliminary evidence suggests that the executive functioning of OO children and HFA children is similar to that of their TD peers under optimal testing conditions. Differences in parental responses on the BRIEF suggest that in everyday situations, IQ-matched TD children were particularly good at executive skills, commensurate with their above average IQ's, while OO children scored below the TD peers, but solidly in the average range. Scores of the HFA children were at-risk for most index scores of the BRIEF, and fell in the clinically significant range for their ability to transition between activities.

112.113 113 Is It a Girl or a Boy? Adaptive Coding of Gender in Children with Autism. E. Pellicano*[1], E. Jaquet[1], L. Jeffery[2] and G. Rhodes[2], (1)*University of Bristol*, (2)*University of Western Australia*

Background: Recent research suggests that face-coding mechanisms are generally flexible or "adaptive". For example, repeated exposure (adaptation) to a series of female faces makes an androgynous face more likely to be judged as male. A recent study, however, has reported that children with autism show reduced adaptation (i.e., shift in perception) to changes in facial identity compared to age- and ability-matched typical peers. This finding suggests that adaptive face-coding mechanisms may be disrupted in individuals with the condition. In addition to these possible difficulties with adaptation, there is also evidence to suggest that the processing of social information in faces, including gender, may be atypical in children with autism. **Objectives:** In this study, we investigated the possible relationships between adaptive difficulties and abnormalities in processing social cues from faces within children with autism. Specifically, we sought to determine whether children with autism would experience less adaptation to gender categories than typically developing children. **Methods:** Ten cognitively-able children with autism (M age = 11 years 10 months; 2 girls) and 10 typically developing children (M age = 11 years 8 months; 2 girls) of similar age and nonverbal ability were assessed on a gender adaptation task. Faces used in the task were morphed faces, which ranged from "female" (80%

female / 20% male) through to "ambiguous" (50% female / 50% male) through to "male" (20% female / 80% male). Each face was presented one at a time and children were asked to decide whether each face was a "girl" or a "boy". During adaptation, children were exposed to either a 100% male or a 100% female face for 30 seconds. After adaptation, the set of morphed faces was again rated for whether each face looked more like a girl or a boy with regular 5 second top-up adaptation. **Results:** Although both groups of children showed a significant adaptation effect in the expected direction, children with autism showed considerably reduced adaptation than their typical peers (i.e., aftereffects were significantly smaller for children with autism). This finding suggests that neural mechanisms coding social information such as gender in faces might be less flexible in children with autism. Baseline gender discrimination did not differ between the groups. **Conclusions:** This study provides converging evidence that adaptive face-coding mechanisms of both identity and gender information may be atypical in autism. Since adaptive mechanisms are ubiquitous in perceptual systems, these findings raise the intriguing possibility that weakened adaptive processes could extend beyond faces and be a general property of autism.

112.114 114 Delayed Self-Recognition in Children with Autistic Disorder and Asperger's Disorder: Evidence for a Temporally Extended Self. C. Dissanayake*[1], J. Shembrey[1] and T. Suddendorf[2], (1)*La Trobe University*, (2)*University of Queensland*

Background: While clear evidence exists for the ability of children with autism to recognize themselves in real time, assessed via mirror self-recognition, little is known of their ability to recognize themselves over time. Temporal self awareness, as assessed via the delayed self-recognition (DSR) task, has been postulated to be associated with the ability to metarepresent. This ability, assessed using standard false belief tasks, is characteristically impaired in children with Autistic Disorder. However, those with Asperger's Disorder are more able to pass false belief tests.

Objectives: The objective in the two studies reported here was to explore delayed self recognition in children with Autistic Disorder and Asperger's Disorder relative to one another and to their typically developing peers. A secondary aim was to establish whether performance on DSR was related to the ability to pass false belief tasks. Children's affective response to their marked image was also explored to distinguish between 'physical' and 'psychological' self awareness.

Methods: Three groups of male children aged between 5- to 9-years comprising 15 children with high functioning Autistic Disorder (HFAD), 12 children with Asperger's Disorder (AspD), and 15 typically developing (TD) children, participated in Study 1. Study 2 included younger children aged 4- to 7-years (18 HFAD and 18 TD). All children participated in a self recognition mark test using delayed video feedback, and a test of false belief. Affective responses displayed by the children when viewing the marked video image of themselves was also coded. Results: Children with HFAD, AspD and the TD children were equally able to use delayed video feedback to recognise themselves, independent of their performance on the test false belief, and their ability to use personal pronouns. Furthermore, no differences were found in their affective responses to their marked video image.

Conclusions: The results cast doubt on the proposed metarepresentational basis for the development of a temporally extended self, with children in all groups showing intact self recognition. Despite some deficits in false belief understanding and the use of pronouns, the children with HFAD were able to not only show delayed self recognition but they also showed positive affect when confronted with their marked image, as did the TD children indicating a level of psychological, in addition to physical, self awareness. Moreover, the finding that children with AspD and HFAD performed similarly on the DSR task adds to the increasing evidence that these conditions are not distinct diagnostic entities.

112.115 115 Determining Implicit and Explicit Contributions to Sequence Learning in ASC. J. Brown*[1], B. Aczél[1], L. Jiménez[2] and K. Plaisted Grant[1], (1)*University of Cambridge*, (2)*University of Santiago*

Background:

There does not appear to be a *general* ASC-deficit in implicit learning, as evidenced by preserved performance on a variety of implicit learning tasks (Brown et al., 2008; Barnes et al., 2008; Kourkoulou et al., 2008; Travers et al., 2008). However, the fact remains that ASC-deficits have been occasionally observed on different versions

of implicit learning tasks (Klinger et al., 2007; Mostofsky et al., 2000).

The authors hypothesise that ASC-deficits on implicit learning tasks arise from atypical explicit learning contributions. For example, Mostofsky et al., (2000) found an ASC-deficit on the Serial Reaction Time (SRT) task using conditions that have been subsequently shown to involve the use of explicit learning processes (completely reliable sequences and long inter-stimulus-intervals - Destrebecqz & Cleeremans, 2001). In contrast, equivalent ASC performance has been identified (e.g. Brown et al., 2008) using conditions that tend to prevent explicit learning (Destrebecqz & Cleeremans, 2001). We examine our hypothesis by comparing ASC and TD children on a SRT-task using completely reliable (deterministic) sequences.

An additional feature of the design allows the mechanism of the atypical explicit contribution to be explored: the sequence information will be embedded within another implicit learning design, Contextual Cueing (CC). Vazquez (2008) developed this hybrid (SRT-CC) design and found that for most sequences, both sequential and contextual learning emerge and remain entirely unaffected by the presence of the other. However, when the sequence is deterministic, contextual cueing is reduced. It is assumed that the reduction of the CC-effect is contingent upon explicit knowledge of the sequence. Concordantly, there is evidence of explicit knowledge from the SRT generation task only when the sequence is deterministic. It has previously been demonstrated that there is intact performance in ASC individuals on the classic (non-hybrid) CC-task (e.g. Barnes et al., 2008). Therefore, if we observe the predicted ASC-deficit on this deterministic-SRT, then we can make inferences about the explicit contribution to SRT-learning from ASC performance on the CC-component of the task. If the CC-effect is superior in the ASC-group, it suggests that the ASC-group acquired less explicit knowledge of the sequence and the deterministic-SRT ASC-deficit stems from the fact that they are worse at learning such tasks explicitly. However, if the CC-effect is reduced equivalently in both groups, then this would suggest that the ASC-group acquired an equivalent amount of explicit sequence knowledge. This would imply that the previously unaffected implicit contribution to SRT-performance in ASC-individuals becomes relatively impaired only in the presence of explicit knowledge.

Objectives:

To test our hypothesis that ASC-deficits on implicit learning tasks arise when there is an atypical explicit learning contribution. Insofar that our hypothesis is true, the design will elaborate the mechanism of the atypical explicit contribution in ASC.

Methods:

The performance of children with ASC is compared with that of TD children matched for IQ and chronological-age (11-14 years-old) on a deterministic SRT-task embedded within a CC-design. Participants also complete post-test generation tasks.

Results:

At the time of writing, data-collection for ASC-participants was incomplete.

Conclusions:

As above, so not possible.

112.116 116 Behavioral Evidence for Atypical Spatial Filtering Properties in Autism : Enhanced Sensitivity for High-Spatial Frequency Information. J. Bertrand-Rivest*[1], L. Kéïta[1], J. Faubert[2], L. Mottron[1] and A. Bertone[1], (1)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (2)*Université de Montréal*

Background: It is becoming increasingly evident that autism differs from other neurodevelopmental conditions, given recurrent demonstrations of superior performances on several tasks (cognitive and/or low-level perceptual) where local or detailed information processing is advantageous (reviews: Mottron & Burack, 2001, Mottron et al., 2006; Berhmann et al., 2006; Happé & Frith, 2006). However, few studies have attempted to systematically assess the spatial filtering properties of early visual mechanisms in autism.

Objectives: To characterize early spatial information processing in autism by measuring contrast sensitivity functions for both luminance- and texture-defined spatial information, reflecting the connectivity of local neural networks (i.e., spatial filters) mediating static processing.

Methods: Spatial frequency tuning was assessed by measuring contrast detection thresholds to luminance- (with and without noise) and texture-defined sine-wave gratings (in gaussian envelope) of different spatial frequencies (0.5, 1, 2, 4, 8 cycles per degree [cpd]) for autistic and typically developing groups. Contrast sensitivity (1/threshold) functions (CSFs) were plotted for each group across conditions.

Results: Results demonstrate an enhanced sensitivity to luminance-defined (no-noise) gratings of high-spatial frequency (8 cpd) in the autistic group. In addition, when normalized, average peak sensitivity for the autistic group was higher (≈ 3cpd) than that of the typical group (≈2cpd).

Conclusions: Consistent with recent electrophysiological evidence (Milne et al., 2008; Mimeault et al., 2008), results of these experiments suggest that low-level static information processing is atypical in autism, and that local stimulus-driven neural networks underlying spatial filtering properties are altered, favoring the analysis of high-spatial frequency (or detailed) information. We suggest atypical lateral connectivity (i.e., enhanced lateral inhibition) within early visual areas as the most plausible type of neural alteration consistent with the behavioral data. The implication of these local network changes on larger-scale atypicalities mediating socially-related perceptual processing will be discussed.

112.117 117 Generativity Abilities Predict Communication Deficits but Not Repetitive Behaviors in Autism Spectrum Disorders. T. N. Holtzclaw*[1], G. Dichter[2], K. S. L. Lam[3], L. Turner-Brown[3] and J. Bodfish[3], (1)*University of Alabama*, (2)*University of North Carolina*, (3)*University of North Carolina at Chapel Hill*

Background: The executive dysfunction theory of autism spectrum disorders (ASD) suggests that repetitive behaviors may be linked to impaired executive function, specifically generativity and inhibition. Individuals with ASD often demonstrate impaired generativity, although findings on the relationship to autism symptomatology have been inconsistent. One study found that impaired generativity was correlated to repetitive behaviors (sameness behavior and circumscribed interests), but another study found that generativity was not related repetitive behaviors, but rather communicative abilities.

Objectives: The present study evaluated generativity using two ideational fluency tasks in children with and without ASD. We hypothesized that the ASD group would be characterized by deficits on both generativity tasks, and that generativity scores would be correlated with symptoms of repetitive behaviors in individuals with ASD.

Methods: The generativity measures consisted of the Use of Objects task and an Animals Fluency Task. Participants included 39 children with ASD and 42 typically developing children aged 6-17 years with an IQ above 70. Autism symptoms were measured using parent questionnaires including the Social Communication Questionnaire (SCQ), the Children's Communication Checklist, 2nd edition (CCC-2), and the Repetitive Behavior Scale-Revised (RBS-R). Diagnosis of ASD was confirmed by the Autism Diagnostic Interview-Revised.

Results: Groups differed significantly on three of four metrics from the Animals Fluency Task and five of seven metrics from the Use of Objects task. Overall, the ASD group gave fewer total and correct responses and a trend towards more redundant responses on the Objects task and more repetitions on the Animals task. In the ASD sample, no significant relations were found between generativity and repetitive behaviors (as measured by the total and subscale scores on the RBS-R). Significant relations were found between performance on the Animals Fluency Task and communication symptoms (as measured by the CCC-2 total exclusive of items assessing social deficits and repetitive behaviors).

Conclusions: Results replicate reports of generativity deficits in ASD and suggest that impaired generativity may reflect communication deficits that are characteristic of the disorder.

112.118 118 Episodic Autobiographical Memory, Time Perception and Self-Awareness in ASC. L. Maister* and K. Plaisted Grant, *University of Cambridge*

Background: Recent research has suggested individuals with ASC have a specific episodic memory deficit with preserved semantic memory functioning. Cognitive capacities such as self-awareness and subjective time perception are considered to play important roles in episodic memory. Studies have shown abnormalities in both these areas in ASC (e.g. Hurlburt, Happe et al. 1994; Szelag et al. 2004), however no study

has yet investigated the relationship between these abnormalities and the episodic memory impairment reported in ASC.

Objectives: The purpose of this research is to investigate episodic autobiographical memory in ASD using both a quantitative measure and a qualitative measure. We then investigate reflective self-awareness and subjective time perception.

Methods: The performance of children with ASC (n = 16) on a quantitative (fluency) and a qualitative (interview) measure of episodic and semantic autobiographical memory was compared to that of typically developing children matched for IQ, generativity and verbal fluency. Their performance on a retrospective time reproduction task (using durations between 500ms and 45s) and a self-awareness task requiring reflection on own knowledge was also measured.

Results: The quantitative memory measures revealed that the children with ASC reported significantly fewer episodic autobiographical memories than typically-developing children. Conversely, there was no difference in the quantity of semantic autobiographical memories recalled between the two groups.

In the timing test, the children with ASC were significantly less accurate in reproducing temporal durations than the comparison group, both at short durations of 500-2000ms (thought to involve attentional processes) and at longer durations of 30-45s (thought to involve long-term memory, in particular the episodic system).

In the reflective self-awareness measure, the ASC group was significantly less accurate in reporting the strength of their knowledge and in differentiating between knowing and guessing. The group also showed a lower correlation between strength of knowledge and the level of confidence in that knowledge than the comparison group.

Conclusions: We conclude that ASC children recall fewer episodic autobiographical memories than comparison children, despite showing no difference in their semantic autobiographical memory recall. In addition, they show time perception and self-awareness abnormalities, which may be correlated with their episodic memory deficits.

112.119 119 Category Formation in Autism: Can Individuals with Autism Form Categories of Dot Patterns. H. Z. Gastgeb*[1], E. M. Dundas[1], N. J. Minshew[2] and M. S. Strauss[1], (1)*University of Pittsburgh*, (2)*University of Pittsburgh School of Medicine*

Background: Categorization is a critical cognitive ability that reduces demands on memory and allows individuals to focus on important aspects of objects while ignoring irrelevant details. In fact, it is such a basic ability that infants are able to form categories of dots, objects and faces within the first year of life (e.g., Bomba & Siqueland, 1983; Rubenstein, Kalakanis, & Langlois, 1999; Strauss, 1979; Younger, 1985). There is a growing amount of evidence suggesting that individuals with autism have difficulty with some aspects of categorization and engage in different categorization processes than do typically developing individuals (e.g., Gastgeb, Strauss, & Minshew, 2006; Klinger & Dawson, 1995; Plaisted, 2000). A recent study by Gastgeb et al. (2006) found that individuals with autism can readily categorize objects (e.g., cats and chairs) when the task involves simple and typical objects but have difficulty when categorization is more complex or involves less typical objects. It is not yet known whether these categorization differences are present during category formation.

Objectives: To examine whether individuals with autism and typically developing individuals differ in their formation of artificially designed categories of dot patterns varying in typicality (i.e., amount of distortion from a prototype).

Methods: High functioning adults, adolescents and children with autism (8-45 years old) and age and IQ matched controls were tested in a category formation task with dot patterns varying in typicality from typical (low distortion of a prototype) to atypical (high distortion of a prototype). During the learning phase, participants were shown high distortion dot patterns. After a delay period, participants were presented with new low distortions, new high distortions, and dot patterns from a new/different category (i.e., high distortions of a different dot pattern prototype). For each dot pattern, participants responded as to whether the dot pattern was a member of the category that they saw earlier or a member of a different/new category.

Results: The autism group differed from the control group in the typicality structure of the categories they formed and in the strength of their category boundaries. The control group showed a pattern of more accurate categorization of low (typical) distortions than high (less typical) distortions. Even though the autism group showed this pattern, they did so to a lesser degree. The control group also evidenced clear category boundaries by accurately excluding the non-category members from the learned category. However, the autism group evidenced more fuzzy boundaries by excluding more high distortion category members and including more non-category members into the learned category.

Conclusions: Individuals with autism did not seem to abstract typicality structures of the dot patterns and evidenced particular difficulty categorizing members at the boundary of a category (i.e., less typical/highly distorted members). They also formed less well-defined category boundaries. The results of this study parallel Gastgeb et al (2006) suggesting that individuals with autism have categorization difficulties with respect to natural and artificially designed categories.

112.120 120 How Do Individuals with ASD Process and Copy Ambiguous Figures?. M. L. Allen* and A. Chambers, *Lancaster University*

Background: The ability to switch between two interpretations of an ambiguous figure (e.g. rabbit/duck) is a well-documented perceptual phenomenon. Children with Autism Spectrum Disorder (ASD) can process these 'reversals' when explicitly told about the ambiguity, however they tend not to do so spontaneously (Mitchell and Ackroyd, 2003; Sobel, Capps and Gopnik, 2003). One way to implicitly examine the understanding of multiple representations is to ask participants to copy the same ambiguous figures under different contextual conditions. If a figure is labelled a 'duck', one might draw something 'duck-like' even if the target stimulus is equally representative of a rabbit. Given the tendency for individuals with ASD to be unbiased by contextual information ('weak central coherence'; Frith, 1989), an alternative possibility is that they may create accurate pictures which more closely represent the target, regardless of context. Objectives: The purpose of the present study was to 1) determine if the ability to experience a spontaneous reversal affects drawing accuracy; 2) explore if labeling affects drawing accuracy; and 3) replicate research suggesting that children with ASD are unlikely to make spontaneous reversals. Methods: Twelve adolescents with ASD (CA 15.2, MA 9.0) were matched to 12 adolescents with learning difficulties (CA 14.6, MA 8.6) on language ability assessed by the BPVS-II. In the Unlabelled condition, 2 ambiguous pictures were individually presented. For each trial, the participant was asked initially to copy the target picture, then probed for spontaneous or prompted reversal, and asked again to draw the target picture on a different sheet of paper. If reversal did not occur it was classed as 'Refusal' and the alternative interpretation was demonstrated. The Labelled condition was similar except the target image was initially named before the individual made any drawings (e.g. can you draw this duck?). A control trial in each condition followed the same procedure but consisted of unambiguous line drawings, to ensure that responses to the test questions were not due to demand characteristics. Each participant received both conditions. Results: The pictures were scored by an independent, blind rater to determine similarity of the drawings of each target image before and after reversal. Drawings by individuals with ASD were more similar to each other than drawings by the control group in the Labelled condition ($t = 2.49$, $df = 23$; $p = 0.02$), but not in the Unlabelled condition ($t = 0.41$, $df = 23$; $p > 0.05$). Both groups showed mostly prompted reversals (44% ASD, 52% control), followed by spontaneous reversals (35% ASD, 33% control), then refusals (21% ASD, 15% control), a non-significant difference. Conclusions: These results suggest that adolescents with ASD are not influenced by contextual information (labels or experience of dual interpretations) when copying ambiguous drawings. That is, their pictures were more similar to each other and to the target picture. Consistent with prior research, individuals with ASD showed mostly prompted reversals, which did not differ from learning disabled peers. This research has implications for how individuals with ASD understand multiple representations and suggests that these individuals have a relative strength in accurate 2-D copying.

112.121 121 Autistic Disturbances of Affective Contact: Are Cognitive Accounts Sufficient?. S. B. Gaigg* and D. M. Bowler, *City University, London*

Background: It is now well established that individuals with Autism Spectrum Disorder (ASD) experience often very marked difficulties in multiple aspects of reciprocal emotional

communication. Controlled laboratory experiments show that such individuals either experience difficulties in identifying the emotional expressions of others or that they deploy qualitatively different perceptual processes in order to do so. In naturalistic settings individuals with ASD tend to direct few emotional expressions at others and when others direct such expressions at them, they often react atypically or not at all. Despite the consistency with which these abnormalities are demonstrated, there is, to date, no consensus as to what the cause of this facet of the ASD phenotype might be. Some argue that socio-emotional disturbances are the result of abnormalities in the development of mentalising abilities, whilst others believe that the core problem lies in the development of relatively basic emotional processes. The only consensus that has emerged over the past few years is that abnormalities of the amygdala most likely play a role in the socio-emotional characterisation of the ASD phenotype.

Objectives: To suggest that recently accumulating evidence from studies assessing emotional processes outside the immediate context of social cognition may help to resolve the debate regarding the developmental origin of socio-emotional disturbances in ASD.

Methods: First, we will demonstrate that it is difficult (if not impossible) to resolve the developmental debate surrounding the socio-emotional disturbances characterising ASD on the basis of evidence from studies that assess the emotional competencies of individuals with ASD solely within the reciprocal social context. We then present an overview of how the concept of 'emotion' is currently operationalised outside the field of ASD in order to highlight a consensus that emotional experiences and behaviours are the result of the interplay between physiological response mechanisms and cognition. Finally, we note that this interplay is known to involve the amygdala at a neural level, establishing a parallel between neural frameworks of emotion and neural frameworks of ASD. On the basis of this overview we conclude that studies of how physiological and cognitive aspects of emotional experiences are integrated in ASD are essential in order to arrive at an understanding of the causes of the clinically defining manifestations of this disorder.

Results: We provide an overview of the few studies that have examined how physiological aspects of emotional experiences influence cognition and behaviour in ASD and conclude that the evidence from these studies suggests that also outside the reciprocal social context, individuals with ASD are characterised by abnormalities in emotional processes.

Conclusions: We will conclude that purely cognitive explanations are inadequate to account for the observation that ASD is characterised by abnormalities in emotional processes outside the social domain and that, as a result, the suitability of such explanations for the socially relevant emotional deficits of ASD is questionable. We present an alternative theoretical framework that we believe is neurologically and developmentally plausible and that could potentially explain not only the social but also the non-social characteristics of the ASD phenotype.

112.122 122 Imitation-Dependent Visuomotor Sequence Learning in ASD. L. R. Dowell*[1] and S. H. Mostofsky[2], (1)*Kennedy Krieger Institute*, (2)*Kennedy Krieger Institute, Johns Hopkins University School of Medicine*

Background: Motor imitation deficits, hypothesized to be a key feature of autism spectrum disorder (ASD), affect learning of communicative gestures (e.g. waving) and may contribute to social impairments associated with the disorder. There have been inconsistent findings regarding visuomotor sequence learning in ASD. However, due to the nature of imitation deficits in ASD, visuomotor sequence learning may be particularly impaired in imitation-dependent contexts.

Objectives: To examine the effect of imitation on visuomotor sequence learning in autism.

Methods: Experiment 1 - 10 children with ASD and 8 typically developing (TD) children completed a standard Serial Reaction Time Task ("Standard SRTT") in which subjects used the fingers of their right hand to push one of four buttons corresponding to red squares on a computer screen. Experiment 2 - 11 children with ASD and 17 TD children completed an imitation-dependent version of the SRTT ("Imitation SRTT"), in which subjects used the fingers of their right hand to push one of four buttons in imitation of a video of a left hand facing the subject. The tasks in Experiment 1 and 2 included 7 blocks of 80 trials; blocks 2-5 and 7 comprised an implicit

10-trial repeated sequence; blocks 1 and 6 were random. For both experiments, learning was assessed using a repeated measures ANOVA (RM-ANOVA) to examine for a decrease in reaction time across blocks 2-5.

Results: Experiment 1 - RM-ANOVA revealed a significant effect of block across the two groups of subjects ($F = 9.9$, $p = .0009$). There was no significant effect of diagnosis across blocks ($F = .63$, $p = .44$). There was no significant interaction effect of block with diagnosis ($F = .28$, $p = .84$); follow-up within-group analyses revealed a main effect of block for TD ($F = 18.7$, $p = .0038$) and ASD ($F = 5.1$, $p = .035$), indicating that both groups showed evidence of learning. Experiment 2 - RM-ANOVA revealed no effect of block across the two groups of subjects ($F = 1.7$, $p = .2$). There was no significant effect of diagnosis across blocks ($F = .07$, $p = .8$), nor was there an interaction effect of block with diagnosis ($F = 1.5$, $p = .2$). Within-group analyses, however, revealed the HFA group showed a distinctly different pattern (much flatter learning curve) than the TD group, such that there was a main effect of block for TD children ($F = 4.4$, $p = .02$), but not for children with ASD ($F = .04$, $p = .99$); this suggests that while TD children showed learning similar to that seen with the Standard SRTT, children with ASD did not.

Conclusions: The findings suggest that children with ASD exhibit impaired motor sequence learning under conditions involving action understanding, such as imitation. This would suggest that, for children with autism, abnormalities in circuits comprising inferior parietal (important for perceptual representations of movement), premotor (important for preparing motor action) and superior temporal sulcal (important for self-other mapping) regions may contribute to difficulties with acquisition of skilled gestures, including those important for socialization/communication.

112.123 123 The Level and Nature of Autistic Intelligence II: What about Asperger Syndrome?. L. Mottron*[1], I. Soulières[1], M. A. Gernsbacher[2] and M. Dawson[1], (1)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (2)*University of Wisconsin-Madison*

Background: Autistic children and adults score on average 30 percentile points higher on the pre-eminent fluid intelligence test, Raven's Progressive Matrices (RPM), than on widely used Wechsler subtest batteries (WAIS-III, WISC-III), while typical individuals do not display this discrepancy (Dawson et al., 2007). Unlike individuals diagnosed with autism, individuals diagnosed with Asperger syndrome do not, by diagnostic definition, present with delays in speech production. Also, individuals diagnosed with Asperger syndrome are, by diagnostic definition, all characterized by intelligence test scores in the normal range, whereas individuals diagnosed with autism may score in any range. Although testing with RPM does not require extensive speech production and comprehension, typical individuals are proposed to rely on language processes to perform many RPM items (Lohman, 2005). How the performance of Asperger adults and children on RPM compares with their Wechlser performance remains uncertain. Preliminary findings have shown that Asperger children (ages 6-12yrs) obtain significantly higher raw scores on RPM than typical children matched on age and Wechsler performance (Hayashi et al., 2008).

Objectives: This study aimed to replicate and extend findings concerning the performance of autistic individuals on RPM in a population of strictly (rather than clinically) defined Asperger children and adults.

Methods: The child sample included 23 Asperger and 24 typically developing children, matched on age (6 to 16 years old). The adult sample included 29 Asperger and 19 control adults, matched on age (16 to 49 years old). An Asperger diagnosis was given for participants eligible for an autism diagnosis on ADI-R or ADOS (module 3 or 4), but who did not have delayed speech, echolalia, pronoun reversal, or stereotyped speech, all as defined in the ADI-R. All participants completed the standard version of RPM. In addition, children completed the Wechsler Intelligence Scale for Children (WISC-III), whereas adults completed the Wechsler Adult Intelligence Scale (WAIS-III). The three instruments were administered by clinicians unaware of the hypotheses of this study.

Results: Asperger children obtained on average a Wechsler Full-Scale IQ at the 48th percentile and a RPM score at the 60th percentile. Planned one-way analyses of variance revealed a significantly higher RPM performance than Wechsler FSIQ performance by the Asperger children, but no difference between performance on the two tests

by the control children (Wechsler FSIQ 70th percentile and RPM at 72nd percentile). Similarly, Asperger adults scored significantly higher on RPM (75th percentile) than on the Wechsler FSIQ (49th percentile), whereas there was no significant difference between performance on RPM (82nd percentile) and Wechsler FSIQ (75th percentile) for the control adults.

Conclusions: These findings demonstrate that, while differing from autistics in history of speech delay and in individually having Wechsler scores in the normal range (here with group averages near the 50th percentile for children and adults), Asperger children and adults are similar to autistic children and adults in presenting with significantly higher RPM than Wechsler scores. These findings suggest that strengths in RPM performance and therefore in fluid reasoning are pervasive across the autistic spectrum.

112.124 124 Attention, Executive Function, and Response Inhibition in Autism Spectrum Disorders. R. Mutreja*, *Texas Tech University*

Background:

Autism spectrum disorders (ASD) involve impairment of attention and executive

functioning. ASD develop at an early age and may affect social, communicative and cognitive development (Sigman, Spence, & Wang, 2006). ASD involves restrictive, repetitive behaviors and social and communicative deficits. ASD usually appears within the first three years of life (Johnson & Myers, 2007). Recent research estimates six per one thousand individuals have ASD. ASD is more prevalent with a 4.3 to one male to female ratio (Newschaffer et al., 2007). Between fifty and seventy percent of individuals with ASD have an intelligence quotient under 70 (Sigman et al., 2006).

Attention is a key cognitive component in learning and cognition. Attention relates to the ability to focus selectively and maintain concentration. Learning is most effective when one is attentive. Poor attention can be a sign of behavior disorders and learning related disorders. Attentional problems are also becoming detectable at a younger age and have been found to correlate with low academic achievement. Thus, attention is an important part of a cognitive system which is crucial to learning.

Executive functioning refers to processes such as planning, inhibition, initiation, mental flexibility, monitoring behavior, set-shifting, working memory and impulse control. ASD is a neurodevelopmental condition that involves impairments in executive function.

Objectives:

The current study aimed to investigate cognitive abilities between individuals with and without ASD. The study looked at attention, inhibition, planning, and spatial reasoning. Individuals with ASD are unique in their abilities and this study sought to explore these cognitive skills and the impact on learning.

Methods:

The *Child Attention Network Test (ANT),* a *Spatial Reasoning Task*, the *Tower of Hanoi*, and the *Directional Stroop Test* were used to test different cognitive abilities including attention, spatial reasoning, planning and inhibition respectively in both ASD and neurotypically developing individuals. Fifty-eight non-ASD, neurotypical children and fifteen children with ASD between the ages of five and eleven performed all four tasks.

Results:

Children with ASD showed low orient attention reaction times, low executive attention accuracy, low inhibition accuracy, quicker reaction time on the inhibition task, and poor accuracy and longer reaction times on the abstract reasoning task.

Conclusions:

The current study used the child ANT on an ASD sample, which has not been previously done. The findings indicate areas of cognitive weaknesses in individuals with ASD and how that may contribute to poor academic achievement. Furthermore, the findings provide possible strategies on improving performance such as direct instruction, increased time, and cues.

Another outcome from this study is the evidence of learned helplessness in individuals with ASD. Learned helplessness is a problem which parents and educators need to address. When students with ASD are unable to perform a task, they seek help and give up on themselves on succeeding at

the task. Learned helplessness is a result of lack of self-confidence, lack of motivation, poor problem solving, poor attention and a feeling of hopelessness. This may result in students falling behind in school.

112.125 125 A Study of Attentional Networks in Individuals with Autism Spectrum Disorder. B. Keehn*[1], A. J. Lincoln[2], R. A. Müller[3] and J. Townsend[4], (1)*San Diego State University / University of California, San Diego*, (2)*Alliant International University*, (3)*San Diego State University*, (4)*University of California, San Diego*

Background: Individuals with autism spectrum disorder (ASD) exhibit early and pervasive abnormalities in attention. It has been suggested that impairments in modulation of attention may underlie the development of sociocommunicative deficits in ASD. We implemented the Attention Network Test (ANT) developed by Fan and colleagues (2002) to investigate three distinct attentional networks: alerting, orienting, and executive control.

Objectives: To examine the efficiency of alerting, orienting, and executive control networks using the ANT in children with ASD and typically-developing (TD) children. Additionally, we sought to investigate the relationship between sociocommunicative deficits and the efficiency of each attentional network.

Methods: Participants were 18 high-functioning children with ASD and 16 age- and NVIQ-matched TD children. Each trial began with a fixation cross presented alone for a variable duration (400-1600ms). With the cross remaining on the screen, a cue (no cue, center, double, spatial) appeared for 100ms, followed by a fixation cross presented for 400 ms. Finally, a target, i.e., an arrow pointing left or right flanked on each side by arrows either pointing in the same direction (congruent condition), the opposite direction (incongruent condition), or bars without arrowheads (neutral condition), appeared above or below the fixation cross. Participants' task was to respond as to whether the center arrow pointed left or right. Three 96-trial blocks were administered. Alerting, orienting, and conflict attentional network scores were calculated by a series of cognitive subtractions following the analysis procedures of Fan et al. (2002).

Results: Groups did not differ in error rate. The ASD group evidenced significantly reduced efficiency of the orienting, but not the alerting or executive, network. Correlations for the ASD group revealed an association between the efficiency of the alerting and orienting networks and sociocommunicative impairments, as measured by the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 1999) and the Social Responsiveness Scale (SRS; Constantino & Gruber, 2005). In addition, efficiency of the executive control network was directly related to IQ scores in the ASD, but not the TD, group.

Conclusions: The results provide further evidence of an impairment in the visuospatial orienting network in children with ASD. Additionally, correlations between the alerting and orienting networks and sociocommunicative deficits suggest that domain-general impairments in attention may be associated with development of ASD symptomatology.

112.126 126 Multisensory Selective Attention: Evidence of Enhanced Performance Facilitation in ASD with the Introduction of Distractor-Target Intervals. N. Russo*[1], J. A. Burack[2], L. Mottron[3] and B. Jemel[4], (1)*The Children's Research Unit (CRU), Program in Cognitive Neuroscience,City College of New York*, (2)*McGill University*, (3)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (4)*Research, Lab, Neurosciences, and, Cognitive, Electrophysiology*

Background: The temporal coincidence of two stimulus events in two different modalities is automatically integrated by the brain of typically developing individuals (TD) even if one of the stimuli is irrelevant to the task at hand. This multisensory integration leads to patterns of behavioral performance (reaction time: RT) that are relatively predictable and related to temporal characteristics of the stimuli to be integrated (e.g. the temporal window of integration). In contrast, individuals with autism spectrum diagnoses (ASD) may show temporal binding deficits (e.g. Brock, et al., 2002; Molholm, et al, IMFAR 2008) and greater performance benefits when provided with more time to process stimuli (e.g. Landry et al., in press; Russo et al., IMFAR, 2008). Here we assay multisensory selective attention abilities in ASD and TD individuals in cases where the target (e.g. visual) and distractors (e.g. auditory) could occur simultaneously or at a delay of 450m.

Objectives: To examine the ability of ASD individuals to selectively attend to one modality (e.g. visual) in the presence of distractors from a different modality (e.g. auditory) and to test the effects of a 450ms delay between the distractor and the target on performance.

Methods: 13 ASD and 13 IQ, gender, and handedness matched TD persons completed a RT multisensory selective attention task. Participants had to detect the spatial location (left or right) of targets in one modality (e.g. visual) in the presence of distractors from a different modality (e.g. auditory). The distractors and target could either be spatially congruent (both were presented on the same side) or incongruent (presented to opposite sides). Targets and distractors could occur either simultaneously or with a 450ms delay between the presentation of the distractors and the subsequent presentation of the target. Distractors were presented on 90% of trials, whereas 10% of trials included no distractor so that comparisons could be made to unisensory attention. The dependent measure was reaction time (RT).

Results: When targets and distractors were presented simultaneously, performance was similar between the groups. However, significant group differences emerged in the delay conditions. When targets were visual, the presentation of an auditory distractor 450ms prior to the target slowed the performance of TD participants by approximately 120ms, but facilitated the performance of the ASD group by 75ms. When targets were auditory, the presentation of a visual distractor 450ms prior to the target improved the performance of both groups but the improvements in the ASD group were greater by 150ms than in the TD group.

Conclusions: The pattern of performance between participants with ASD and TD persons were similar when targets and distractors were presented simultaneously, but ASD individuals demonstrated greater performance gains in delay conditions than TD participants. These findings support the notion of a longer temporal window of multisensory integration in ASD and will be discussed with respect to theories of cognitive and perceptual processing in ASD.

112.127 127 Attention and Cross-Modal Integration in Children with Autism Spectrum Disorder. B. Keehn*[1], M. Westerfield[2], A. J. Lincoln[3] and J. Townsend[2], (1)*San Diego State University / University of California, San Diego*, (2)*University of California, San Diego*, (3)*Alliant International University*

Background: Cross-modal integration is a critical prerequisite to the development of higher-level cognitive functions, including language and social communication. However, information sharing between auditory and visual modalities and between sensory and attentional domains appears to be severely impaired in individuals with autism spectrum disorder (ASD).

Objectives: To evaluate the effects of attention on cross-modal integration in children with ASD.

Methods: Participants were 17 high-functioning children with ASD and 15 age- and NVIQ-matched typically developing (TD) children. Stimuli consisted of pictures and sounds of animals or musical instruments. For each trial, a sound and picture were presented together in either a matched or mismatched condition. Matched trials consisted of either a picture of an animal or instrument paired with a congruent sound (e.g. a picture of a dog with a 'bark' sound; congruent condition). Mismatched trials consisted of a picture of an animal or instrument paired with a cross-category sound (e.g. a picture of a dog with a violin sound; incongruent condition). Participants completed two separate tasks using identical stimuli described above: (1) they were asked to respond as to whether the picture was an animal or an instrument (visual attention task) and (2) they were asked to respond to whether the sound and the picture were matched or mismatched (integrated attention task). Participants were instructed to respond as quickly as possible without making mistakes.

Results: Groups did not differ in error rate in either experiment. For the visual attention experiment, there was a marginally significant interaction between stimulus congruency and group. Follow-up ANOVAs on the incongruent-congruent difference scores revealed that the ASD group had significantly larger difference scores as compared to the TD group. Additional single-sample t-tests showed that difference scores for the ASD group, but not the TD group, were significant.

For the integrated attention experiment, there was no significant stimulus congruency by group interaction. Follow-up ANOVAs revealed no significant group differences for incongruent-congruent difference scores. Single-sample t-tests showed that difference scores for both groups were significant. For the ASD group, there was a significant correlation between difference scores and ADOS algorithm scores for the visual attention but not the integrated attention condition.

Conclusions: Results for the visual attention experiment suggest that for the TD group top-down, inhibitory filtering may preclude cross-

modal integration of audio-visual stimuli. However, the ASD group evidenced a significant slowing in the incongruent relative to congruent condition, indicating that the top-down inhibitory filter may be impaired. Results of the integrated attention experiment suggest that both ASD and TD children demonstrate cross-modal integration. Finally, divergent outcomes between the two experiments as well as the significant relationship between difference scores and ASD symptomatology suggest that attention plays an important role in cross-modal integration in both TD and ASD.

112.128 128 Being the Subject of Another's Attention; Differences in Skin Conductance Levels in Children with High-Functioning Autism and Asperger Syndrome. S. Stagg*, P. Heaton and R. Davis, *Goldsmiths College, University of London*

Background: Children with autism spectrum disorder (ASD) show hyper-arousal to direct eye contact (Kylliäinen and Hietanen, 2006). Increased level of arousal may in part explain why avoidance of the eye region is common in some children with ASD. Whilst eye contact in itself may not be arousing to typically developing individuals, being the object of another person's attention is. This is may induce greater levels of self awareness in typically developing adults (Hietanen et al., 2008). Some children with ASD avoid contact with others although it is not known whether such contact is associated with low or high levels of arousal. Low levels of arousal to others in early infancy may result in the child with autism paying less attention to others and also have a detrimental effect on early language development.

Objectives: This study investigated whether children with an ASD displayed similar patterns of arousal to typical controls when the subject of another's direct attention. It further examined the scores of children with a diagnosis of high-functioning autism (HFA) and Asperger Syndrome (AS) on the same measure and investigated possible associations between these scores and measures of language ability.

Methods: 30 children with ASD and 18 typical controls took part in the study. The ASD group were further analysed by dividing the group into HFA (11) and AS (13) categories based on language onset criteria. Galvanic skin conductance measures were used to record arousal in children during a 10 second viewing of a face looking directly at them or a face looking toward another face and away from the participant. Measures on the Vineland Adaptive Behaviour Scale and the British Picture Vocabulary Scale were used to study associations between language and arousal measures.

Results: Overall skin conductance responses (SCR) were higher for typical controls than for the ASD group. Similarly the AS group also showed significantly higher SCRs than the HFA group. Both the control and the AS group demonstrated higher SCRs when they were the object of another's attention although this was not significant for the control group. In contrast, the HFA displayed no difference in SCRs between these two conditions. Correlational analysis demonstrated a trend towards higher SCRs being associated with better language skills.

Conclusions: The study suggests that, when compared to typical controls, children with ASD demonstrate hypo-arousal when they are the subject of another's attention. Further, children with HFA demonstrate similarly low levels of arousal whether they are the object of another's attention or not. In contrast, the AS group displayed similar patterns of arousal to the control group. It is suggested that normative levels of arousal may be an important mechanism of early joint attention in children with ASD and may play a role in the language onset differences displayed in children with AS and HFA.

112.129 129 The Effects of a Modified Learning Strategy on the Mathematical Word Problem Solving Ability of Middle School Students with High Functioning Autism. P. Schaefer Whitby*[1] and G. R. Mancil[2], (1)*University of Central Florida*, (2)*Kelly Autism Program at Western Kentucky University*

Background: Children with HFA/AS are outperformed by their neurotypical peers on mathematical problem solving skills even though they have average-to-above-average intelligence (Dickerson Mayes & Calhoun, 2003b), have average-to-above-average computation skills (Chiang & Lin, 2007), and are educated in the general education setting (Twenty Sixth Annual Report to Congress, 2004). In order to graduate with a regular diploma, all students must take and pass three high school mathematics courses including algebra I. Students with HFA/AS present with a unique set of cognitive deficits that may prevent achievement in the mathematics curriculum, even though they present with average mathematical skills.

Objectives: Determine the effectiveness and efficiency of the use of a modified learning strategy to increase the mathematical word problem solving ability of children with high functioning autism or Asperger syndrome.
Methods: The subjects were referred by local teachers who serve students with autism spectrum disorders. The subjects' diagnosis of ASD was confirmed by a review of records and the completion of the ADI-R. Academic achievement subtest scores for reading comprehension and mathematical computation were completed to identify the current level of functioning. The Mathematical Problem Solving Assessment- Short Form was administered to determine the need for word problem solving intervention. The subjects were then taught mathematical word problem solving using the Solve It! curriculum during non-content course time at their schools. Generalization data was collected in the subject's regular education mathematics classroom. Sessions were videotaped, work samples were scored, and then graphed using a multiple baseline format. Three weeks after the completion of the study, maintenance data was collected. If subjects did not maintain a high use of the strategy, they were entered into the second study to determine if a IPOD video prime or written prime served best to increase word problem solving.
Results: The results of the study indicate a functional relationship between the use of the Solve It! strategy and the percent correct on curriculum based mathematical word problems. The subjects obtained efficient use of strategy use in five training sessions and applied the strategy successfully for five acquisition sessions. Percent correct on mathematical word problems ranged from 20% during baseline to 100% during training and acquisition trials. Error analysis indicated reading comprehension interference and probable executive functioning interference. Students who did not maintain strategy use quickly returned to intervention using a video prime.
Conclusions: Findings of this study show the utility of a modified learning strategy to increase mathematical word problem solving for students with high functioning autism and Asperger syndrome. Results suggest that priming is a viable intervention if students with autism do not maintain or generalize strategy use.

112.130 130 Randomized Study Contrasting Behavioral and Naturalistic Approaches to Inducing Speech in Prelinguistic Children with Autism Spectrum Disorders: Preliminary Analysis.

B. Reichow*[1], R. Paul[2], E. Schoen[1] and M. Lewis[1], (1)*Yale Child Study Center*, (2)*Yale University School of Medicine*

Background:

Autism and related disabilities are severe disorders of development, disrupting social relationships, communication, play, adaptive skills, and academic skills. These disruptions often lead to life-long disability. The development of functional spoken language by the end of preschool is known to be related to improved outcomes in this syndrome. Although many different approaches to developing speech in prelinguistic children with autism have emerged, there is a lack of systematic research comparing these approaches.

Objectives:

This poster presents early findings from a study comparing the effectiveness of two intervention strategies (behavioral and naturalistic) in children with autism spectrum disorders (ASD). The behavioral approach (i.e., direct speech-focused treatment) to be studied is Rapid Motor Imitation Training (RMIT; Tsiouri & Greer, 2002), and the naturalistic approach is Prelinguistic Milieu Teaching (PMT; Yoder & Warren, 2002).

Methods:

Participants were randomly assigned to one of the two treatments. The following inclusion criteria were used: (a) children had a diagnosis of an ASD, (b) child was between 36 - 72 months-old, (c) produced fewer than 10 different words in spontaneous speech, (d) could imitate simple motor actions, and (e) had expressive communication levels below 18 months. Treatment sessions were delivered by a SLP 3 times per week for 12 weeks. Treatment fidelity was continuously monitored throughout treatment sessions by off-site experts, and remained high across interventionists and sessions.

Results:

Preliminary data analyses of pre- and post-treatment measures consisting of 3 participants from each group were conducted. Analyses of the children's scores on the *MacArthur-Bates Communication Inventories-3rd Edition* (Fenson et al., 2007), the Communication and Symbolic Behavior Scales (Wetherby & Prizant, 2002), and

the *Mullen Scales of Early Learning* (Mullen, 1995) were conducted. In examining the difference between the pre-treatment and post-treatment assessments, all children receiving treatment made improvements during the course of the treatment. Improvements were seen in the frequency and diversity of words spoken during the assessment session, the diversity of words parents reported the child was using, and the number of words the parents reported the child understood. Anecdotal records also indicated the children receiving treatment increased their ability to imitate gestures and simple actions, which is often considered a prerequisite skill for the acquisition of spoken language. Results of six-month follow-up assessments are pending, and will be presented. An additional comparison with a no treatment contrast group consisting of 3 individuals not meeting the motor imitation inclusion criteria are also being analyzed, and these data will also be presented.

Conclusions:

Given the preliminary nature of the data, it is too early to determine the superiority of one treatment. However, the results suggest multiple types of treatment delivered with high fidelity can be beneficial to young children with autism with limited verbal communication skills.

112.131 131 The Impact of Augmentative and Alternative Communication on the Development of Functional Communication Skills in Individuals with Autism Spectrum Disorders: a Meta-Analysis of Intervention Research from 1976-2008. O. Wendt*[1], R. Schlosser[2] and L. L. Lloyd[1], (1)*Purdue University*, (2)*Northeastern University*

Background:

Approximately 14-25% of children diagnosed with ASD present with little or no functional speech and are candidates for augmentative and alternative communication (AAC). AAC replaces or supplements natural speech and handwriting through aided or unaided, alternative forms of communication such as, for example, manual signs and gestures, graphic symbols, and speech-generating devices (SGDs). AAC interventions aim to develop communication skills such as requesting, natural speech production, and social communicative behaviors.

Objectives: To evaluate the existing experimental research literature and to review the evidence for the effectiveness of AAC in ASD.

Methods: Meta-analytic procedures were applied to aggregate and evaluate intervention studies. Meta-analysis is a statistical reviewing technique that provides a quantitative summary of findings across an entire body of research. This meta-analysis involved the following elements: (a) an extensive literature search containing computerized database searches, hand-searches in professional journals, and ancestral searches; (b) stringent inclusion criteria to ensure only experimental studies of methodological rigor entered the meta-analysis; (c) a pilot-tested coding protocol plus reliability analysis on both study inclusion and coding; (d) aggregating intervention outcomes statistically by conducting separate analyses for group and single-subject design data and implementing adequate effect size metrics for each, i.e., Cohen's d and Hedges' g for group studies and Percentage of Non-overlapping Data, Improvement Rate Difference and Percentage of Pairwise Data-Overlap for single-subject studies.

Results: A total of 43 single subject and 2 group studies met the inclusion criteria. These studies involved a total of 118 participants, the majority of which was between six and ten years old, diagnosed with autism and no functional speech. Meta-analysis of pooled effect sizes yielded the following results.

☐Functional requesting skills: AAC interventions based on unaided approaches such as gestures and manuals signs showed equal effectiveness when compared to interventions based on graphic symbols. Both are significantly more effective than using SGDs.☐

Natural speech production: When increasing vocalizations was the target outcome, manual signs, the Picture Exchange Communication System (PECS), and SGDs, yielded mixed results of effectiveness regardless of intervention type. Increasing imitative speech yielded higher effect sizes compared to spontaneous speech, and aided language stimulation appeared to be superior to PECS training in targeting these outcomes.☐

Social-communicative behaviors: PECS was found to be "highly effective" for increasing cooperative play, joint attention, and eye contact.

Conclusions: The use of graphical symbols for the teaching of requesting offers the most solid

empirical evidence. Research however, has not reached a level at which it could productively inform choices of one graphic symbol type over others. Manual signs and gestures might play a bigger role if they were part of a multimodal communication system while being mindful of their limitations. Research is lacking on effective strategies for teaching conditional use of manual signs. Speech production data seem independent of how well a child has acquired the introduced AAC modality. Research needs to investigate how acquiring different AAC modalities is related to effectiveness in speech production.

112.132 132 Is Language Regression Related to a Theory of Mind?. A. Lukowski*, N. Basehore, K. Osann, M. M. Abdullah, A. R. Ly and W. A. Goldberg, *University of California, Irvine*

Background:

Regressive autism is characterized by the loss of acquired language and social skills at approximately 18 to 24 months in addition to a diagnosis of an autism spectrum disorder (ASD). Many studies have attempted to explain the different developmental trajectories between children with regressive and non-regressive autism; however, the phenomenon of regressive autism continues to be poorly understood. Because deficits in theory of mind are characteristics of autism, it is important to determine if and how children with regressive autism demonstrate differences in theory of mind compared to children with ASD but without regression. To our knowledge, this is the first study to examine theory of mind in relation to regression in children diagnosed with ASD.

Objectives:

The primary goal of the present research was to examine whether children with ASD who had and had not experienced early language regression differed in their performance on traditional theory of mind tasks.

Methods:

Thirty-three children with ASD from a national study also participated in this substudy. Families were mostly Caucasian, middle-class, and well-educated. ASD diagnoses were made independently. Based on the ADI-R, 18 children had experienced early word loss; 15 had not. At a mean age of approximately nine years, children completed a battery of theory of mind tasks: appearance-reality tasks (including nonverbal), first-order false-belief tasks, and positive and negative belief-desire tasks. Each task was administered twice. For each set of theory of mind tasks, children received a score of zero for failing both assessments, a score of one for passing one of the two assessments, and a score of two for passing both assessments. The number of times a child succeeded on both assessments across the various tasks was used to create a composite score with a maximum value of six.

Results:

After examining receptive language as a possible covariate, ANOVA was used to determine whether children with language regression performed differently from those without language regression on each set of theory of mind tasks and the composite score. Results indicated that children who reportedly had language regression performed better on the nonverbal appearance-reality questions (M = 1.57, SE = .15) relative to children who had not experienced language regression (M = 1.12, SE = .13; $F(1, 27) = 4.73$, $p < .03$); other task scores and the composite score did not differ between groups.

Conclusions:

These study findings suggest that the presence of early language abilities may facilitate performance on some aspects of theory of mind, particularly those requiring nonverbal responses. One possible interpretation is that the children with early access to language may have been able to learn about certain aspects of communication before the regression occurred, whereas children with persistent deficits in language from early in life may not have had this opportunity. Although replication with a larger sample is needed, this work contributes to the literature on cognitive differences in children with ASD by indicating that variability in performances across tasks exists as a function of the presence or absence of regression early in life.

112.133 133 Diagnostic Differentiation of Autism Disorders and Pragmatic Language Impairment. L. M. Reisinger*[1], K. Cornish[2], E. Fombonne[2], J. A. Burack[2] and L. Tidmarsh[2], (1)*Montreal Children's Hospital*, (2)*McGill University*

Background: The diagnostic and clinical differentiation between children with autism spectrum disorders (ASDs) and children with pragmatic language impairment (PLI), two

populations that share a similar linguistic profile, was examined in school-aged children. Charting the behavioral and cognitive profiles of these populations can serve to aide diagnostic differentiation and educational intervention. **Objectives:** The objectives of this study were two-fold. One, to compare scores on diagnostic measures of autism between school-age children with ASD and those with PLI. Two, to investigate differences between children in these groups and typically developing children in the areas of social cognition and executive function. **Methods:** The participants included 22 school-aged children diagnosed with ASD (mean age = 10.2 years), 19 children with PLI (mean age = 9.6 years), and 35 typically developing comparisons (mean age = 10.5 years) matched on language age and IQ. All the participants were verbal and had an IQ above 80. In study 1, the participants with ASD and PLI were tested on the Autism Diagnostic Observation Schedule (ADOS) and the Social Communication Questionnaire (SCQ). In study 2, the participants in all three groups were tested on the measures of three hierarchical levels of Theory of Mind, a planning measure, and a response inhibition measure. **Results:** There was a significant difference between diagnostic groups in the level of severity of behaviors represented by the Communication and Reciprocal Social Interaction sub-domains on both diagnostic measures. However, in the sub-domain of repetitive and rigid behaviors, the difference between groups was subtler and not useful as a differentiating factor. While both the children with ASD and those with PLI violated more rules on the 'planning in problem-solving' task than the typically developing group, only the children in the ASD group demonstrated impaired functioning on the planning measure. The findings of this study suggest that children with PLI may be more vulnerable than children with ASD to developmental lags in understanding false belief but less vulnerable to impairments in planning and monitoring behavior. **Conclusions:** The diagnostic differentiation between ASD and PLI is complex, especially in school-age populations. Behavior symptoms may be more subdued in school-age children and thus should not be used as a tool for diagnostic differentiation. Social communication delays are generally more severe in children with ASD, with some children with PLI presenting with comparable levels of severity. Educational planning for these two populations must be informed by both group similarities (e.g. difficulty forming theories about the beliefs and desires of others in order to predict future behavior) and differences (e.g. planning in problem solving) in cognitive and social development. Thus, the development of individual education plans should be created within the general framework of known areas of strengths and weaknesses related to diagnostic categorization and then further tailored to childrens' personal profiles based on an assessment of skills.

112.134 134 Use of Evidentials in Turkish-Speaking Children with High Functioning Autism. S. Tek* and L. Naigles, *University of Connecticut*

Background: Turkish is an agglutinative language, with a rich and regular morpho-syntactic system. One of the structures of this system, the indirect evidential –mis, requires both syntactic and pragmatic knowledge to be used properly. Syntactically, –mis is produced after the verb but negation and/or tense/aspect markers can intervene (compare Ali gelmis = 'Ali come + evidential marker' = Ali came, apparently with acmayacakmis = '(He) + open + negation + future + evidential marker' = He will not open, evidently). As a full syllable, -mis is a perceptually salient morpheme. Pragmatically, –mis conveys indirect past experience, which is based on inference or hearsay, and encodes information which happens outside conscious awareness. Thus, the indirect evidential –mis presupposes presence of theory of mind skills, which are necessary to attribute mental states to oneself and to others. The interplay between the pragmatic and morpho-syntactic systems in Turkish makes -mis an interesting structure to study with individuals with high functioning autism, because these individuals have mostly intact grammatical skills coupled with impaired social-pragmatic skills. Objectives: Investigate the use of the indirect evidential –mis in Turkish high functioning children with autism, as a salient grammatical structure that taps into theory of mind abilities. Methods: We tested five children with high functioning autism (mean age = 9.4 years, SD = 3.78). Our control group consisted of four children with Down syndrome (mean age = 11.5, years SD = 2.38), and five typically developing children (mean age = 6.3 years, SD = 2.33). Children were administered a wordless picture book: "Frog, where are you?", and were told to tell the story that they saw in the pictures. Children's performance was videotaped, and the number of times children used the indirect

evidential –mis, as well as their total mean length of utterance in morphemes (MLU), were calculated from the videotapes. Results: Children in all three groups did not differ from each other in their MLUs (M(ASD) = 4.18, M(DS) = 4.20, M(TYP) = 4.23). In contrast, children in all three groups significantly differed from each other in their use of the indirect evidential -mis, $\chi 2$ (2) = 7.66, $p < .05$. Children with autism produced significantly fewer utterances with –mis (M = 1.5) than both the typically developing children (M = 27.4) Mann-Whitney U = 1.00, $p < .05$, and the children with Down syndrome (M = 27.0), Mann-Whitney U = 1.50, $p < .05$. No significant differences were found between the typical and the Down syndrome groups. Conclusions: High-functioning children with autism have difficulty with the indirect evidential –mis, demonstrating how pragmatic skills in Turkish influence aspects of morpho-syntactic development.

112.135 135 A Comparison of the Effect of Object and Gesture Imitation Training on Language Use in Children with Autism. K. Lalonde* and B. Ingersoll, *Michigan State University*

Background: Research indicates that children with autism have deficits in imitation that may underlie the abnormal development of other social-communicative behaviors. It has been shown that imitation is associated with the development of language (Bates et al., 1988). Reciprocal Imitation Training (RIT) is a developmentally-based imitation intervention that teaches imitation within a social-communicative context. RIT is effective at teaching children with autism spontaneous, generalized object and gesture imitation. In addition, across studies, changes in object (Ingersoll & Schreibman, 2006) and gesture (Ingersoll, Lewis, & Kroman, 2007) imitation were associated with concomitant increases in verbal imitation and spontaneous language, suggesting that teaching non-verbal imitation can improve language behaviors. Research suggests that object and gesture imitation skills are independent and that gesture imitation is more closely associated with language skills (Stone, Ousely, & Littleford, 1997). However, it is not clear if teaching gesture imitation to young children with autism improves language more than object imitation.

Objectives: This study examines 1) whether children are more likely to engage in verbal imitation during object or gesture imitation training using RIT, and 2) whether adding gesture imitation training improves the overall rate of appropriate language use in children with ASD who have already been participating in object imitation training.

Methods: **:** Four children with autism participated in this study. The children ranged in age from 35 to 47 months at intake with mental ages ranging from 22 to 30 months on the Bayley Scales of Infant Development, 2nd edition (Bayley, 1993). Expressive language age ranged 21 to 23 months (Total language 18 to 21 months) on the Preschool Language Scale Fourth Edition (Zimmerman, Steiner & Pond, 2002). Participants received training in object and gesture imitation using RIT in three, 20-minute sessions per day, three days a week for 10 weeks. This study used a rapidly alternating treatments design to examine whether teaching object or gesture imitation using RIT leads to greater use of verbal imitation. It also used a multiple-baseline design across the same children to examine whether adding gesture imitation training improves the overall rate of appropriate language use in children with ASD who have already been participating in object imitation training.

Results: Preliminary results indicate children were more likely to use verbal imitation during gesture than object imitation training. Further, children showed greater improvements in their use of appropriate language after gesture imitation was begun.

Conclusions: Teaching gesture imitation using naturalistic behavioral treatment to child diagnosed with autism appears to directly increasing language use. These findings may have important implications for both language development and early intervention.

112.136 136 Conversation in High-Functioning Autism: Do Linguistic and Pragmatic Features Vary Depending on the Topic Being Discussed?. A. Nadig*[1], I. Lee[2], L. Singh[2] and S. Ozonoff[3], (1)*McGill University*, (2)*Boston University*, (3)*M.I.N.D. Institute, University of California at Davis Medical Center*

Background: Individuals with high-functioning autism, despite performing well on standardized language tests, have considerable difficulties with social communication. Previous research found that young children with autism (Tager-Flusberg&Anderson,1991) and school-aged children with autism (Capps,Kehres,&Sigman,1998) produced fewer responses that were relevant to and contingent upon their conversational partners' utterances,

than did matched children with developmental delays, reflecting problems with topic maintenance and discourse coherence.

Objectives: Conversational interaction is an understudied topic that has significant import for daily functioning. This study adds a novel dimension to the empirical research in this area: do linguistic and pragmatic features of conversation change depending on the topic of discussion? We compared conversations on generic topics (siblings, pets) with those on motivated topics (circumscribed interest or favourite hobby). Motivated topics may improve topic maintenance by increasing participants' level of engagement. Alternatively, they could engender more atypical language use and monologue-like discourse, given the isolating nature of circumscribed interests.

Methods: Participants were 21 children with high-functioning autism (HFA) and 17 typically-developing comparisons matched on age (9 to 13 years), language level, and Performance IQ. They participated in brief, semi-structured conversations with an adult partner, on both a generic topic and a motivated topic. Verbal exchanges were transcribed from video and coded using a scheme that quantified numerous linguistic and pragmatic aspects of the exchange. Reliability was established on the coding scheme between two coders blind to group membership. We predicted the HFA group would display problems with topic maintenance (e.g. fewer contingent responses, more self-contingent elaborations), problems providing an appropriate amount of information (rather than over- or under-informative statements), more atypical utterances (e.g. scripted or pedantic speech, unusual word choice), and less use of mental state terms than the comparison group. No specific predictions were made about the effect of topic.

Results: The overall number of participant utterances, adult utterances, and proportion of participant to adult utterances, did not differ between groups. For the **generic topic**, both groups produced a similar amount of contingent responses. However, the HFA group produced significantly more grammatical errors ($p<.05$) than comparisons. For the **motivated topic**, the HFA group provided significantly fewer contingent responses than comparisons ($p<.05$). Those responses that were contingent still differed from those of the comparison group, in that they expressed inappropriate levels of information ($p=.01$). For **both topics**, the comparison group generally provided elaborations that were contingent on the topic their partner had introduced, whereas the HFA group provided elaborations that were self-contingent on their own prior utterances ($p<.05$); this tendency was stronger for the motivated than the generic topic. In addition, atypical utterances were observed significantly more often in the HFA group, whereas mental state terms were observed significantly less often than for comparison participants.

Conclusions: Some communicative differences (more atypical utterances, fewer mental state terms) were observed across conversational topics, while motivated topics specifically led to decreased topic maintenance and more monologue-style speech by the HFA group (as observed by fewer contingent responses, inappropriate levels of information in contingent responses, and heightened use of self-contingent elaborations).

112.137 137 Do You See What I'm Saying? Deficits in the Visual Enhancement of Speech Comprehension Under Noisy Environmental Conditions in Autism. J. J. Foxe*[1], L. A. Ross[1], D. Blanco[1], D. Saint-Amour[2] and S. Molholm[3], (1)*City College of New York*, (2)*CHU Sainte-Justine Research Centre*, (3)*The Children's Research Unit (CRU), Program in Cognitive Neuroscience,City College of New York*

Background: Viewing a speaker's articulatory movements substantially improves a listener's ability to understand spoken words, and this is especially so under noisy environmental conditions. In this study we investigated the ability of children with autism to effectively integrate visual and auditory speech. Multisensory integration deficits have long been theorized in ASD but as yet, very little empirical work actually exists to support this notion.

Objectives: Our objective was to determine to what extent children with ASD experience benefit from visual articulation and to detail under what listening conditions they might show the greatest audiovisual multisensory impairments.

Methods: We assessed the ability to recognize auditory-alone and audiovisual speech embedded in different levels of background noise in 7 high functioning children with autism and compared

their performance with that of 12 age-matched typically developing children. We used a large set of monosyllabic words as our stimuli in order to closely approximate performance in everyday situations.

Results: Children with autism showed clear deficits in their ability to derive benefit from visual articulatory motion. This multisensory impairment was most pronounced at the lowest signal-to-noise levels. That is, at the lowest levels of background noise, ASD children were the least affected and did show evidence of multisensory integration, whereas their performance was impacted to a progressively greater degree as the level of background noise was increased.

Conclusions: These results reveal a specific deficit in multisensory speech processing in children with autism and suggest that this multisensory deficit is greatest when the environment is at its noisiest or most confusing. We conclude that multisensory integration dysfunction is likely an important aspect of autism spectrum disorder (ASD).

112.138 138 Do Children with Autism Show Collaborative Competence in Dialogue?. J. A. Hobson*[1], P. Hobson[2], F. Larkin[3] and A. Tolmie[3], (1)*Institute of Child Health, UCL*, (2)*University College London and Tavistock Clinic, London*, (3)*Institute of Education*

Background: It is widely acknowledged that verbally able individuals with autism have difficulty in adapting their language to pragmatic context (e.g. Gernsbacher, Geye, & Weismer, 2005; Tager-Flusberg, Paul, & Lord, 2005). In the case of conversations, speakers and listeners need to monitor each other for understanding and interest, interpreting and offering cues as feedback on each other's contributions. A variety of non-verbal, verbal and paralinguistic features are used to manage this pragmatic dimension of conversational interchanges so that turns of talk are organized, maintained and shared. Although there is evidence that non-verbal aspects of conversational exchanges such as head-nodding while listening are atypical among individuals with autism (García-Pérez, Lee, and Hobson, 2007), conversational management (or grounding, see Clark, 1996) has received little investigation among individuals with autism.
Objectives: The aims of this study were to evaluate how children with and without autism collaborate in a conversation with someone else using verbal, nonverbal and paralinguistic cues, and to explore what this might reveal about inter-subjective contributions to conversational competence. To this end, we applied novel ratings of communication grounding to assess collaborative competence in dialogue.

Methods: Participants were 18 verbally able children and adolescents with autism and an age and language-matched comparison group of 18 children and adolescents without autism, all between the ages of 7 and 15. Participants were administered the Autism Diagnostic Observation Schedule (ADOS), Module 3, a semi-structured, standardized assessment of communication and social interaction (Lord, Rutter, DiLavore & Risi, 2002). This assessment provides 35 – 40 minutes of conversational interaction between the participant and an examiner who presents numerous social presses to elicit conversation and dialogue. Videotapes of the ADOS administration were rated according to a novel rating scale (the Collaborative Competence in Dialogue Scale, CCDS) to assess the presence and quality of seven collaborative features in conversation: continuers, assessments, appropriate next response, try markers, gaze to regulate, gaze to co-regulate, and repairs.
Results: Participants with and without autism were equally likely to include continuers, assessments, appropriate next responses, and try markers in their conversations. However, with the exception of assessments, each of these was rated as markedly atypical in the autism group. Furthermore, participants with autism were less likely to use gaze to regulate, gaze to co-regulate, and repairs. It was rare for any of the collaborative features to be rated as both present and typical (and to enhance conversation effectively) among the participants with autism. Collaborative cues tended to appear in rote and/or intermittent forms.
Conclusions: Verbally able individuals with autism have pragmatic difficulties that go beyond understanding and producing context-relevant speech. They also have problems with conversation management and collaboration in dialogue. Drawing on constructs from conversation analysis, this study suggests that limitations in interpersonal engagement may underlie many of the atypicalities in conversation observed in autism.

Special Interest Group Program

113 Sleep and Autism

Organizers: B. A. Malow[1]A. Richdale[2](1)*Vanderbilt University*, (2)*La Trobe University*

113.00 Sleep - Special Interest Group. B. A. Malow*[1] and A. Richdale[2], (1)*Vanderbilt University*, (2)*Olga Tennison Autism Research Centre*

Sleep difficulties affect many children and adults with autism spectrum disorders and may have a negative impact both on their behaviour and their families. These sleep difficulties have many causes, including neurochemical, behavioral, and secondary to co-morbid medical (encompassing also neurological and psychiatric) disorders and their treatments. Improving sleep may benefit daytime functioning in these individuals. The presence and type of sleep difficulties may also serve as an important phenotype for characterization of autism subtypes.

This Special Interest Group will focus on the interface of sleep and autism. Our goals for this year are to begin a dialogue among researchers interested in this area and identify specific areas for study and future collaboration. After the organizers present a brief overview of the topic, participants will break into small focus teams for discussions on specific areas including the nature and causes of sleep difficulties in autism, genetics related to sleep, tools for measuring sleep difficulties, and behavioral and pharmacological treatments. Focus teams will then share their discussions with the larger group. Participants are encouraged to sign up for focus teams on the IMFAR website prior to the meeting.

Keynote Address Program
114 What Would "Better" Diagnoses of ASDs Look Like?"

Speaker: C. Lord*University of Michigan*

114.00 Introduction/Simons Foundation Autism Research Initiative - Gerald D. Fischbach.

114.01 What Would "Better" Diagnoses of ASDs Look Like?.

Invited Educational Symposium Program
115 Neuropathology and Neuroimaging

Organizer: G. Blatt*Boston University School of Medicine*

Speakers: N. J. Minshew[1]G. Blatt[2]D. C. Chugani[3]D. Murphy[4](1)*University of Pittsburgh School of Medicine*, (2)*Boston University School of Medicine*, (3)*School of Medicine, Wayne State University*, (4)*King's College London, Institute of Psychiatry*

115.00 The Continuing Story of Connections in Autism: Truly A Distributed Neural Network Disorder. N. J. Minshew*[1], M. Behrmann[2], C. Thomas[3] and K. Humphreys[4], (1)*University of Pittsburgh School of Medicine*, (2)*Carnegie Mellon University*, (3)*Harvard Medical School*, (4)*Institute of Psychiatry*

As a result of imaging technology, tremendous progress has been made in understanding the mind and brain in autism. The first major contribution was the evidence of increased total brain volume that led to the beginning acceptance of autism as a neural systems disorder. Over the course of a decade, functional magnetic resonance imaging (fMRI) studies generated evidence of functional underconnectivity across neural systems and of increased local connectivity in high functioning individuals with autism. In the last 3-5 years, diffusion tensor imaging studies have provided evidence of both micro- and macro-structural abnormalities in white matter pathways. Recently, fMRI studies have further characterized the cognitive and neural mechanisms underlying language and visual processing deficits in autism with clear implications for intervention. A converging theme across these studies is the lack of the innate specialization of circuitry in autism that is associated with neuronal organizational events. This section will review key findings that advance the definition of the neural basis of autism.

115.01 Alterations in Key GABAergic Biomarkers in Autism: Potential Disruption of Inhibitory Networks. G. Blatt*, *Boston University School of Medicine*

Although autism is a heterogeneous disorder ranging from mild to severe in nature, changes in the GABAergic system is emerging as a consistent neuropathological finding in affected brain areas. An ideal brain region to study these changes is the cerebellum, whose intrinsic GABAergic circuitry forms the foundation of its output to thalamic and cerebral cortical areas. Specifically, in the posterior lateral cerebellar cortex (Crus II region), the density/number of GABA receptors (GABAAR, GABABR and benzodiazepine binding

sites) is altered in adult autism subjects. Furthermore changes in GAD 65 or 67 mRNA have been found in inhibitory neurons in the cerebellar cortex and, in a subpopulation of neurons in the dentate nucleus. These neurons are thought to project back to the inferior olivary complex exerting inhibitory control of its electrotonic coupling of excitatory climbing fiber (CF) responses. Immunohistochemical labeling has shown abnormal accumulation of neurofilaments in some CFs on PC dendrites potentially altering transmitter release. Thus a number of key GABAergic biomarkers have emerged suggesting a cascade of events with strong implications to disrupt olivocerebellar circuitry in adult autism subjects. An interesting development is that some of these biomarkers demonstrate similar alterations across other affected brain areas including the hippocampus, anterior and posterior cingulate cortex (BA 24, 23) and fusiform gyrus (BA 37). This suggests widespread effects of altered inhibitory circuits throughout affected regions in autism.

115.02 Neurochemical Developmental Regulation In Autism. D. C. Chugani*, *School of Medicine, Wayne State University*

Autistic behaviors are associated with multiple etiologies and may, therefore, result in heterogeneous responses to treatment. Regardless of etiology, however, it appears that autism is the consequence of deviations from normal brain developmental processes. Identification and delineation of the timing of these deviations from the normal developmental sequence may allow strategies for pharmacological intervention aimed at setting brain developmental programs back on course. Molecular imaging studies, using techniques such as positron emission tomography (PET), can provide information regarding time course differences in the ontogeny of various neurochemical processes in autism or subgroups of children with autism, and can therefore aid in designing treatment strategies with respect to timing of interventions. For example, studies using α[11C]methyl-L-tryptophan as a PET tracer to estimate serotonin synthesis showed that humans undergo a period of high brain serotonin synthesis capacity during childhood, and that this developmental process is disrupted in autistic children. Since serotonin is known to be an important factor involved in postnatal synaptogenesis, one approach to the treatment of autism would be the use of serotonergic agents in children less than the age of 6 years, when serotonin synthesis capacity is lower in autistic children compared to non-autistic controls. The goal of treatment would be to provide a more normal modulation of synaptic plasticity for a finite period of brain development. This talk will explore strategies for exploiting critical periods for therapeutic alteration of brain development in autism.

115.03 Neuropathology and Brain Imaging – How Can They Inform Each Other ?. D. Murphy*, *King's College London, Institute of Psychiatry*

I will discuss how brain imaging can be used to build on neuropathological evidence for the potential neural substrates of autism spectrum disorders.
In particular I will present work which builds on prior findings from post mortem and peripheral biomarker studies; and which is starting to elucidate the potential role(s) of serotonin and glutamate/GABA. The main imaging technologies presented will be DT-MRI, sMRI, and fMRI.

Oral Presentations Program
116 Motor Function

116.00 Does Motor Skill Competence Distinguish Subtypes of Pervasive Developmental Disorder in a 'High-Functioning' Population of Children?. L. Slator*[1], W. Mandy[2], K. Puura[3], M. Kaartinen[3], M. Murin[4] and D. H. Skuse[1], (1)*Institute of Child Health*, (2)*University College London*, (3)*Tampere University Hospital*, (4)*Great Ormond Street Hospital for Children*

Background:

Motor skills deficits are not core characteristics of Asperger syndrome as defined by DSM-IV-TR, but they are often regarded as being closely associated with the syndrome in the form of clumsiness or dyspraxia. No specific motor skill deficits are described in terms of the diagnostic criteria for autism or PDD-NOS, or their associated characteristics.

Objectives:

We aimed to examine the prevalence of reported delays in motor development, current clumsiness and dyspraxia, in relation to independent clinical diagnoses in a large heterogeneous sample of 'high functioning' children with Asperger syndrome, autism, or PDD-NOS.

Methods:

Data from parental report were analysed for a sample of 987 children (4-16 years, mean age 9.0 yrs) from clinics in London, UK, and Tampere, Finland, which had been subject to comprehensive and standardized autism assessments (including ADI algorithm, ADOS). All subjects had normal-range intelligence. Diagnoses were defined according to DSM-IV-TR criteria, and comprised autism (N=199), Asperger syndrome (N=159), PDD-NOS (N=255), and clinical controls without ASD (N=374). Measures of motor competence included developmental motor milestones, current fine and gross motor skills, and a dyspraxia/clumsiness index. Domains were derived by principal components analysis of a validated parent-report scale.

Results:

Ages at which key motor skills were achieved were significantly later in those diagnosed with autism than in Asperger syndrome, after controlling for IQ. No mean difference was found between the PDD-NOS and Asperger syndrome groups on this variable, but both were significantly delayed relative to controls. The three PDD groups did not differ significantly in terms of mean verbal IQ, nor did they differ in this respect from the controls.

In terms of both fine and gross motor skills, children within the broad category of PDD performed significantly less well than clinical controls. There was no mean difference in any measure of motor competence between children with a clinical diagnosis of autism, and those with a clinical diagnosis of Asperger syndrome, although both groups were significantly more impaired than those with a diagnosis of PDD-NOS.

On the measure of dyspraxia/clumsiness children with autism had significantly more severe symptoms than those with Asperger syndrome. Those with PDD-NOS were similar to the Asperger syndrome group and both the latter groups were more significantly impaired than normal controls.

Conclusions:

A delay in onset of language skills, a defining criterion for autism, is associated with delay in the onset of motor milestones too. By middle childhood, there is no significant difference between children with autism and those with Asperger syndrome in terms of fine or gross motor competence. On a measure of dyspraxia/clumsiness, children with autism are more impaired than those with Asperger syndrome. Accordingly, we found no evidence to substantiate the widely-held assumption that motor clumsiness, or indeed any other measure of motor impairment, is characteristic of children who meet criteria for the diagnosis of Asperger syndrome, compared to those with 'high-functioning' autism.

116.01 Children with Autism Show Enhanced Somatosensory-Guided Motor Learning. L. R. Dowell[1], M. E. Richardson[1], A. J. Bastian[2] and S. H. Mostofsky*[3], (1)*Kennedy Krieger Institute*, (2)*Johns Hopkins School of Medicine, Kennedy Krieger Institute*, (3)*Kennedy Krieger Institute, Johns Hopkins University School of Medicine*

Background: Difficulties with performance of skilled motor gestures is a commonly reported finding in autism spectrum disorder (ASD). Given the developmental context, impairments in motor skill learning may contribute to these findings. In previous studies, children with autism have demonstrated anomalous patterns of motor sequence learning on visually-guided motor tasks, including serial reaction time and rotary pursuit. Whether they show similar impairments when motor sequence learning depends on somatosensory feedback has not been studied.

Objectives: To examine whether children with ASD show impaired motor sequence learning when it depends on somatosensory feedback.

Methods: Nine children with ASD (1 female) and 7 typically developing (TD) children (1 female) ages 8-12 years completed a task in which they used a stylus pen to trace a continuous closed-loop maze composed of linear segments while blindfolded. The task consisted of 4 blocks of trails, with 4 trials in each block. During blocks 1, 2, and 4 subjects traced a primary maze with eight decision points at which they could either make a correct turn or an error into a dead end; during block 3 subjects traced an "interference maze" that was a mirror image of the primary maze. The number of loops completed during each 48 second trial was recorded using a digitizing tablet. Learning was assessed using a repeated measures ANOVA (RM-ANOVA) to examine for an increase in completed loops across trials in primary maze blocks (1, 2, and 4).

Results: RM-ANOVA across trials from blocks 1, 2 and 4 revealed no significant effect of diagnosis on the total number of loops completed ($F=1.6$; $p = .23$). Across both groups of subjects, there was a significant effect of trial ($F = 7.5$; $p = .03$), with the number of completed loops increasing over time. Furthermore, there was significant trial-by-diagnosis interaction effect ($F = 14.6$; $p = .01$), such that children with HFA showed a greater increase in the number of loops completed across trials than did TD children.

Conclusions: The findings, revealing that the HFA group showed significantly greater improvement in performance during blindfolded maze tracing, suggest that children with autism show superior motor learning when it is guided by somatosensory feedback. In contrast, findings from prior studies suggest that visuomotor learning (i.e., motor learning guided by visual feedback) may be impaired in children with autism. The combined results suggest that increased reliance on somatosensory-guided learning may contribute to impaired acquisition of skilled motor gestures (including social and communicative gestures) that are often learned through visually-guided imitation. This has important implications for guiding therapies targeted at improving social and communicative skills and understanding the neural basis of autism-associated impairments in motor, social and communicative development.

116.02 A Link Between Grammar and Dyspraxia in Boys with Autism. M. Walenski*[1], S. H. Mostofsky[2] and M. T. Ullman[3], (1)*San Diego State University*, (2)*Kennedy Krieger Institute, Johns Hopkins University School of Medicine*, (3)*Georgetown University*

Background:

Along with deficits in communication and language that define autism spectrum disorders (ASD), dyspraxia (motor skill deficits) is also commonly observed. It has been proposed that abnormalities of procedural memory may underlie impaired development of motor skill knowledge and grammatical (but not lexical) abilities. Examination of English past tense morphology offers a well-studied contrast between grammatical and lexical aspects of language. Dual-system models claim that regularized past-tenses (*walked*) depend on rule-based grammatical computation (stem + -ed), while irregularized past-tenses (*slept*) depend on memorized word-specific (lexical) knowledge. Thus the former but not the latter is predicted to share a common neurocognitive substrate with motor skill knowledge.

Objectives:

To examine the relationship between grammatical performance (past tense production) and dyspraxia in children with ASD.

Methods:

Sixteen high-functioning boys with ASD (ages 8-15 years) participated in both a past-tense production task and a videotaped praxis examination. For the past tense production task we examined accuracy at producing the past tenses of real regular (*walked*; n=32) and real irregular (*slept*; n=32) verbs. For the praxis measure, we examined mean accuracy (percent correct responses) during performance of gestures-to-command, gestures-to-imitation, and gestures-with-tool-use. Pearson partial correlations between past tense accuracy and praxis accuracy were computed, with age (years) included as the partialled variable (given the potential for age effects in both the past-tense production and praxis measures). The pattern did not change when age was not partialled out of the correlations.

Results:

For the boys with ASD there was a significant positive correlation between mean regular verb and praxis accuracy ($r(13)=0.58$, $p=0.02$); whereas the correlation between mean irregular verb and praxis accuracy was not significant ($r(13)=0.39$, $p=0.15$). Significant negative correlations between regular verb performance and each of the praxis error measures (gesture-to-command, gesture-to-imitation, and gesture-with-tool-use) were also found (all $p<0.05$); whereas, again, none of these correlations reached significance for irregular verb performance (all $p>0.12$).

Conclusions:

The relationship between regular (but not irregular) verb accuracy and praxis scores is consistent with a common neurocognitive substrate for grammar and motor skills, that may underlie impaired performance in both domains in

boys with autism. Specifically, the observed correlations suggest that both may be related to underlying difficulties with procedural memory necessary to acquire these skills.

116.03 Physical Activity and Screen Time in Children with Autism Spectrum Disorders. L. Bandini*[1], J. M. Gleason[1], C. Curtin[1], S. E. Anderson[2], S. A. Cermak[3], M. C. T. Maslin[1] and A. Must[4], (1)*University of Massachusetts Medical School*, (2)*The Ohio State University*, (3)*University of Southern California*, (4)*Tufts University School of Medicine*

Background: Regular physical activity is important to health and well-being; however, physical activity behaviors in children with autism spectrum disorders (ASDs) have received little research attention. We hypothesized that because of social deficits and difficulties with motor skills and communication, children with ASDs would have lower physical activity levels (measured by accelerometry or questionnaire) than typically developing children and would spend more time in sedentary behaviors.

Objectives: To compare objectively measured physical activity levels, time spent in participation in a variety of physical activities, and time spent with electronic media between children with ASDs and typically developing children.

Methods: Fifty-three (53) children with ASDs (44 males/9 females) and 58 typically developing children (45 males/13 females) ages 3-11 (mean age ~6.6 years) participated in the Children's Activity and Meal Patterns Study (CHAMPS). Children wore an activity monitor (accelerometer) for 5 weekdays and 2 weekend days. Parents completed a questionnaire that queried types and duration of children's participation in physical activities and the amount of "screen time," i.e., TV, computer, video games, in the past year.

Results: After adjustment for age and sex, percent time spent in moderate/vigorous activity measured by accelerometry was similar in children with ASDs (21.3%) and typically developing children (22.4%). In contrast, based on questionnaires, children with ASDs participated in fewer different physical activities than did typically developing children (7.1 vs. 9.8, $p<0.001$). Total time spent annually in activities, adjusted for age and sex, was also lower for children with ASDs compared to typically developing children (159 vs. 225 hr/y, $p<0.0001$). For typically developing children, but not for children with ASDs, time spent in physical activity overall increased with age. After adjustment for age and sex, total adjusted weekly screen time was significantly higher in children with ASDs than typically developing children (11.6 vs. 7.2 hr/wk, $p<0.001$).

Conclusions: Children with ASDs are reported to engage in fewer types of activities and for less time than typically developing children. Children with ASDs also spend more time engaged with electronic media ("screen time") than do typically developing children. Contrary to our hypothesis, the contrasting observation that both groups of children engage in similar levels of moderate/vigorous activity as measured by accelerometry, but that children with ASDs engage in fewer physical activities and for less time according to parental report, may indicate that some of the activity in children with ASDs is not captured by standard questionnaire-based measures. In particular, children with ASDs are known to engage in repetitive self-stimulatory behaviors such as hand flapping, spinning, and pacing. Such behaviors may be captured as moderate-vigorous activity by accelerometry although would not likely be reported by parents as time spent in physical activity. Furthermore, children with ASDs may engage in spontaneous activity while watching television or videos. This suggests that exploration of factors associated with physical activity in children with ASDs may require specially developed questionnaires and/or different methodologic approaches.

Supported by NICHD-R21HD48989

116.04 Basal Ganglia Shape Predicts Social and Motor Dysfunction in Boys with Autism. A. Qui[1], D. Crocetti[2], M. C. Adler*[3], M. I. Miller[1] and S. H. Mostofsky[4], (1)*Johns Hopkins University*, (2)*Kennedy Krieger Institute*, (3)*Teachers College at Columbia University*, (4)*Kennedy Krieger Institute, Johns Hopkins University School of Medicine*

Background: Autism is associated with abnormalities suggestive of basal ganglia dysfunction, including stereotyped behavior and abnormalities on motor examination. Neuroimaging investigations of basal ganglia structure have thus far been limited to examination of whole volumes. Large deformation diffeomorphic metric mapping (LDDMM), a powerful computational tool used for detailed analysis of morphology (i.e., shape), can provide a more comprehensive understanding of basal

ganglia contributions to the behavioral features of autism.

Objectives: To apply LDDMM to detailed analysis of basal ganglia structure and its association with the motor and behavioral features of autism.

Methods: Basal ganglia structures (caudate, putamen, globus pallidus) were manually delineated on high-resolution MR images in 32 boys with high-functioning autism (HFA) and 45 typically developing (TD) controls, ages 8-12 years. LDDMM was then used to map between-group differences in shape across each structure and to examine correlations with measures of basic motor skill (assessed using the PANESS – Physical and Neurologic Examination of Subtle Signs), praxis (assessed using a standardized videotaped praxis examination), and core social/communicative/behavior features of autism (assessed using the ADOS-G, Module 3). We examined the group shape differences using principal component analysis and correlation of the basal ganglia shape with behavioral measures using point-wise Pearson's correlation analysis. The overall significance was confirmed via permutation tests.

Results: Group shape differences were principally localized to the right striatum: compared to TD boys boys with HFA showed significant compression, in the right anterior-ventral and posterior-dorsal putamen and in the right anterior caudate and caudate tail; they showed significant expansion in the mid-dorsal putamen, middle caudate, and posterior globus pallidus. Behavioral analyses revealed the HFA group showed significantly poorer performance on the PANESS ($p<0.001$) and praxis examination ($p<0.001$). Brain-behavior correlations revealed that, across the groups of subjects, compression of the bilateral posterior putamen was a significant predictor of poorer performance on the PANESS, while compression of the bilateral anterior putamen was a significant predictor of poorer praxis performance; in both cases these correlations were driven by significant findings in the HFA group (but not controls). For the HFA group, bilateral expansion in the ventral caudate head (nucleus accumbens) was a significant predictor of higher ADOS social domain scores.

Conclusions: For boys with HFA, shape abnormalities in the basal ganglia are associated with motor and social dysfunction. Consistent with established mapping of striatal function, basic motor skill impairment was associated with compression in posterior putaminal regions in circuit with primary sensorimotor cortex, while impairment in performance of skilled gestures (assessed on praxis examination) was associated with compression in dorsal anterior putaminal regions in circuit with premotor cortex. Impaired social function characteristic of autism was associated with expansion in the nucleus accumbens, in circuit with orbitofrontal cortex. The pattern of findings suggests that abnormalities within parallel subcortical circuits may contribute to the motor, social and behavioral features of autism. The detailed level analysis offered by LDDMM may therefore prove valuable in identifying neuroanatomic biomarkers of autism.

116.05 Neural Correlates of Motor-Linked Implicit Learning in Autism Spectrum Disorders. B. G. Travers*[1], C. L. Klein[1], M. R. Klinger[1], L. G. Klinger[1] and R. K. Kana[2], (1)*University of Alabama*, (2)*University of Alabama at Birmingham*

Background:

Motor-linked implicit learning is the learning of a sequence of movements without conscious awareness (e.g., getting faster at typing one's own name as a byproduct of signing emails). Although motor symptoms are frequently reported in persons with autism spectrum disorders (ASD), recent behavioral studies have suggested that motor-linked implicit learning may be intact in ASD (e.g. Barnes, et al., 2008; Müller et al., 2004; Travers et al., 2008). Nevertheless, persons with ASD may recruit different cortical areas while engaging in this type of learning. The serial response task (SRT) is one of the most common measures of motor-linked implicit learning. In neurotypical individuals, the SRT activates the premotor, sensorimotor, primary motor, anterior cingulate, caudate, and medial prefrontal cortices (Destrebecqz et al., 2007). In this study, an SRT experiment was used in an fMRI scanner to investigate the cognitive and neural responses to motor-linked implicit learning in persons with ASD.

Objectives:

The present study sought to examine whether different patterns of fMRI measured brain activation occurred for motor-linked implicit learning in persons with ASD compared to neurotypical controls.

Methods:

Eight high-functioning adolescents and adults with ASD and twelve age and IQ matched controls participated in this study (data collection is ongoing). The data were collected using a Siemens 3T Allegra fMRI scanner. Participants completed an SRT in which they responded with a button press to the picture of an airplane displayed on the screen in one of four possible locations. Unknown to participants, the location of the airplane followed a repeating 12-step sequence of movement. Participants completed 12 alternating blocks of sequenced and non-sequenced trials. There were no breaks or delineations between sequenced and non-sequenced blocks.

Results:

Behavioral results suggest that the participants with ASD demonstrated less motor-linked implicit learning indicated by a smaller reaction time difference between non-sequenced and sequenced blocks in participants with ASD (*M* = +8 ms) than neurotypical controls (*M* = +35 ms). Furthermore, the fMRI results suggest that different cortical areas were recruited by participants with ASD during motor-linked implicit learning. Specifically, participants with ASD showed less bilateral sensorimotor (postcentral gyrus) and primary motor (precentral gyrus) activation than neurotypical controls. However, participants with ASD activated more in the left inferior frontal gyrus than neurotypical controls. These results suggest less motor-specific activation in participants with ASD compared to neurotypical controls.

Conclusions:

Behaviorally, motor-linked implicit learning may be less robust in persons with ASD. At the neural level, people with ASD showed atypical brain responses, especially in terms of less sensitivity to the sequenced blocks of trials in the sensorimotor and primary motor cortices and more sensitivity to the sequenced blocks of trials in the inferior frontal gyrus compared to neurotypical controls. This suggests that persons with ASD may be using more frontal-mediated, explicit and effortful learning rather than motor-mediated implicit learning during the SRT.

Oral Presentations Program
117 Toddlers

117.00 Atypical Activity Monitoring in 20-Month Old Toddlers with and without Autism Spectrum Disorder. F. Shic*[1], J. Bradshaw[1], B. Scassellati[2], A. Klin[1] and K. Chawarska[1], (1)*Yale University School of Medicine*, (2)*Yale University*

Background: Individuals with Autism Spectrum Disorder (ASD) often exhibit difficulties in monitoring the activities of others and attending to contextually relevant aspects of scenes. Proficiency in these abilities in typically developing (TD) toddlers not only reflects advancing expertise in core social skills, such as joint attention, but is also likely to impact future cognitive and social development. Understanding the developmental progression of atypical monitoring in ASD is critical for the design of early diagnostic instruments and targeted intervention.

Objectives: This study examines, through eye-tracking, the differences between the visual scanning patterns of toddlers diagnosed with ASD (age: M=21 (SD=3) months; gender: 22M, 4F; N=26) and typically-developing controls (age: 20(3) months; gender: 20M, 6F; N=26) as they watched a video of a child-adult play interaction.

Methods: Subjects were presented with a 30 second video in which a female adult was directing a male child in the assembly of a child's puzzle toy. The scene took place in a typical office with other toys strewn about the floor. The subjects' viewing patterns were tracked and the time spent examining each of the following areas was recorded: 1) activity area (area of joint focus of the adult and the child, including the puzzle); 2) actors (the adult and the child); 3) toys (not including the puzzle activity); and 4) background (furniture, carpet, etc.). The proportion of time spent looking at these regions was analyzed with a MANOVA with diagnosis (ASD or TD) as a factor.

Results: ASD toddlers monitored the activity area significantly less than TD toddlers (ASD: .43(.2); TD: .56(.15); $F(1,50)=6.6$, $p<.05$) and attended more to the other toys in the scene (ASD: .12(.09); TD: .07(.05); $F(1,50)=8.0$, $p<.01$). No differences were found between ASD and TD toddlers in the proportion of time spent examining the actors or background features. However, in ASD toddlers, nonverbal cognitive scores on the Mullen Scales was positively correlated with activity monitoring ($r=.44$, $p<.05$) and negatively correlated with attention to

the background (r=-.44, p<.05). Attention to the actors was negatively correlated with socialization scores (r=-.53, p<.01), social-communicative impairment (r=-.42, p<.05), and repetitive behavior/restricted interests (r=-.60, p<.01) on the ADOS.

Conclusions: Toddlers with ASD monitor the activities of others in an atypical fashion, attending less to the area of joint focus and shared activity and more to background distracters such as toys. Patterns of abnormal viewing were associated with social and cognitive measures of functioning. These results suggest that, by 20 months, the pathogenic factors involved in ASD are affecting the ability of ASD toddlers to attend to socially relevant areas of scenes. It is likely that, as the ASD toddlers grow older, the cumulative effects of this atypical monitoring will further impair their imitative learning and their ability to acquire knowledge regarding the rules of social interaction and play.

117.01 Subtypes of Toddlers with Autism Spectrum Disorders. L. D. Wiggins*[1] and D. L. Robins[2], (1)*Centers for Disease Control and Prevention*, (2)*Georgia State University*

Background: Identification of subtypes of toddlers with autism spectrum disorders (ASDs) can improve knowledge on early manifestations of the disorders. Moreover, identification of subtypes of ASDs may inform early identification efforts by examining how characteristics that most distinguish subtypes affect performance on common diagnostic instruments. Past research suggests that social relations, verbal abilities, nonverbal abilities, and the presence of certain stereotyped interests and behaviors (SIB) may be important factors in delineating subtypes of ASDs in toddlers. Yet there is no published study that examines empirically derived subtypes in a sample of such young children.

Objectives: To determine whether distinct subtypes can be derived from a sample of toddlers who fail an autism screen and are subsequently diagnosed with an ASD.

Methods: Children were identified by two ongoing screening studies. Families were given the Modified Checklist for Autism in Toddlers (M-CHAT) during a visit to their pediatrician or early intervention provider. Families that indicated risk for developmental delay were offered a comprehensive clinical evaluation. The total sample evaluated (n = 288) was 80% male and 20% female. One hundred and seventy two children had race data; 143 of these children were White, 11 were Black, seven were Hispanic (including Puerto Rican), four were Asian, two were bi-racial, one was Hawaiian, and four chose "other" to describe their race. The average age at time of evaluation was 26 months (range = 13-37 months; *SD* = 5 months). One hundred eighty six children were diagnosed with an ASD after the clinical evaluation. Of these 186 children, 113 were diagnosed with Autistic Disorder, 72 were diagnosed with PDD-NOS, and one was diagnosed with Asperger's Disorder. Items from the Childhood Autism Rating Scale were used to identify subtypes of children subsequently diagnosed with an ASD.

Results: Cluster analysis found three subtypes of toddlers with ASDs. Discriminant function analyses revealed two functions that accounted for group differences: a social-communication function and a SIB function. Group differences were found on social, communication, and cognitive skills and the rate and intensity of certain SIB (e.g., sensorimotor behaviors). Therefore, groups were labeled low social-communication with high SIB, low social-communication with low SIB, and high social-communication with low SIB. Lower-order or sensorimotor SIB that distinguished subtypes were repetitive use of objects and unusual sensory response. Items that assessed higher-order cognitive rigidity did not differentiate subtypes in this sample.

Conclusions: We found three subtypes of toddlers with ASDs delineated by social-communicative maturity and the rate and intensity of lower-order SIB. Consequently, defining toddler subtypes by these factors may improve knowledge of early manifestations of the disorders and early identification efforts. Repetitive use of objects and unusual sensory response should be given utmost priority when classifying toddlers with ASDs since these lower-order SIB distinguished subtypes in our sample. Higher-order SIB that focus on cognitive rigidity have less utility and, therefore, may be less useful in distinguishing ASD subtypes in younger cohorts.

117.02 Perception of Audiovisual Synchrony Under Varying Degrees of Social Context in Infants with Autism. J. B. Northrup*, D. Lin, G. Ramsay, A. Klin and W. Jones, *Yale University School of Medicine*

Background: In recent research, we found that two-year-olds with autism failed to orient towards point-light displays of human biological motion. Rather than giving preferential attention to biological motion, children with autism oriented towards non-social, physical contingencies present within the stimuli—contingencies that were disregarded by control children. These results indicated that a skill present in two-day-old, typically-developing infants, as well as in chronologically-, nonverbally-, and verbally-matched 2-year-old control children, was already atypical in very young children with autism. In its place, these toddlers with autism demonstrated intact processing of a physical contingency: audiovisual synchrony

Objectives: The goal of the current project is to downward extend this line of research to younger infants under more controlled conditions in order to explicate the above finding. Our aims are (1) to assess the sensitivity of infants with ASD to audiovisual synchrony devoid of social context; and (2) to measure the effect of varying social contexts upon the preferential attentional patterns of infants with ASD relative to audiovisual synchronous stimuli.

Methods: Three groups of children – infants with ASD, typically-developing infants (TD), and infants with non-autistic developmental-delays (DD), ages 12-24 months – participated in two series of experiments based on a preferential looking paradigm to split-screen presentations. We used stimuli that varied in degree of social context: pure tones, sine wave speech, and naturalistic speech in the auditory modality, and circles, ellipses and dynamic faces in the visual modality. The first series of experiments tested baseline sensitivities to audiovisual synchrony. The second series of experiments tested how sensitivity to audiovisual synchrony was affected by varying the social context of the stimuli. Eye-tracking technology measured infants' looking.

Results: Preliminary results show that infants with autism are as sensitive as their peers to the perception of audiovisual synchrony. However, audiovisual synchrony detection in infants with autism is less influenced by accompanying social context: while the introduction of biasing social context altered the preferential viewing patterns of TD and DD controls, the change in contextual information did not alter the viewing patterns of infants with ASD.

Conclusions: The present study suggests that in the developmental experience of children with autism, physical contingencies of coincident light and sound are more salient than the surrounding social context. Future investigations will benefit from studies, starting still earlier in life, of the developmental unfolding of such selective learning profiles. Exactly which signals are spontaneously attended to and which are missed, and the consequences thereof for structural and functional brain development, may shed light on the neurobiological anomalies that predispose these altered avenues of learning.

117.03 Does Audiovisual Synchrony Predict Visual Fixation Patterns in 2-Year-Old Children with Autism?. J. Xu*, G. Ramsay, A. Klin and W. Jones, *Yale University School of Medicine*

Background: A recent study found that 2-year-olds with autism spectrum disorders (ASD) looked less at the eyes and more at the mouths of approaching adults, as compared with both typically-developing (TD) and with non-autistic, developmentally-delayed (DD) controls. A parallel study showed that toddlers with ASD failed to give preferential attention to point-light displays of human biological motion, again in contrast with both TD and DD controls. Instead, viewing by the ASD group was predicted by level of audiovisual synchrony (AVS): increased fixation was given to stimuli in which change in movement was accompanied by synchronous change in sound. In control children, viewing was unrelated to AVS. These results raised the hypothesis that, in toddlers with ASD, increased fixation on the mouth and decreased fixation on eyes may be due to increased attention to the synchrony of lip movements and speech sounds.

Objectives: The aim of this study is to determine whether the reduced visual fixation on eyes and increased fixation on mouths in toddlers with ASD is due to underlying preferential attention to physical rather than social contingencies.

Methods: Physical contingencies were identified by quantifying AVS in the eyes, mouth, body, and object regions of naturalistic, child-directed caregiver video stimuli, using techniques modified from the previous study. This approach was utilized to determine whether that for toddlers with ASD, but not for controls, visual fixation patterns to each region would be positively

predicted by level of AVS, both spatially and temporally.

Results: Preliminary results suggest that, when viewing approaching caregivers, visual fixation in toddlers with ASD for a region appears to be correlated with the amount of AVS in that region. In concordance with previous reports, we found that the mouth was both the region with greatest AVS and the region attracting the greatest amount of visual fixation in the ASD group. We also observed that the timing of fixations is correlated with the change in baseline AVS for each region. In contrast, relative AVS does not appear to predict the visual fixation patterns of toddlers in either of the two control groups.

Conclusions: These results, along with the point light biological motion study, suggest that the preferential visual attention of toddlers with ASD is attracted by co-occurrences of change in motion and sound rather than by entreating social-communication signals. These findings, in turn, propose that children with autism may have atypical early experiences that would profoundly impact their development: seeing a face in terms of its physical contingencies but missing its critical social signals. These results may provide for new diagnostic tools and may also reveal an early stage in the development of compensatory and alternative strategies for interaction with others, particularly with respect to language and communication skills.

117.04 Assessing Joint Attention in Autism across Multiple Settings. R. Fadda*[1], E. Sitzia[2] and G. Doneddu[2], (1)*University of Cagliari*, (2)*A.O.B. (Azienda Ospedaliera Brotzu)*

Background: Clinical research indicates that the early impairment of Joint Attention (JA) seems to be central for the disturbance of social development in autism. In particular, young children with autism are characterized by a specific impairment in the capacity for Initiating JA (IJA) and Responding to JA (RJA). Considering that these deficits have been related to social symptom intensity, intervention responsiveness and long term social outcomes in autism (Mundy, 1995), an accurate assessment of early JA abilities in young children with autism might be crucial in order to define more specific and effective interventions.
Objectives: The present study wanted to explore the JA behaviours in young children with autism in multiple contexts and with different tools (direct observation and an interview to the parents), in order to determine how stable these behaviours are across different measures.
Methods: To achieve this aim we examined 20 participants with ASD (14 males; 6 females; aver.chron.age=34 mths; DS=9,56; aver. developmental age=23 mths; ds=8 mths) in the Early Social Communication Scales (Mundy et al., 2003) and in the ADOS. The parents completed the Vineland Adaptive Behavior Scales (VABS).
Results: In general, the children in our sample showed low scores in all the JA behaviors assessed across the two context of observation (ESCS and ADOS) and in the VABS. IJA was significantly correlated with the ADOS communication scores ($r=-0.48$; $p<0.05$) and the ADOS social interaction scores ($r=-0.48$; $p<0.05$). The correlation is pointing in a coherent direction, since high scores in the ADOS indicates a lack of social abilities. IJA correlates also with VABS communication scores ($r=0.55$; $p<0.05$) and VABS socialization scores ($r=0.57$; $p<0.05$). RJA was significantly correlated with all the ADOS and VABS measures except that with the ADOS communication scores ($r=-1.93$; $p>0.05$).
Conclusions: These results confirms that infant's joint attention behaviors reflects a robust aspects of social deficit in autism that is stable across different context of observation and accross different measures (direct vs indirect). They indicated also that different types of joint attention behaviors might be underestimated by classical diagnostic tools, such as the ADOS. For this reason, the assessments conducted in multiple context may provide a more valid measure of the child's joint attention behaviors.

117.05 Early Detection of Autism in Pre-Verbal Children (ADEC). G. Bradshaw, R. L. Young*, P. Williamson and N. Brewer, *Flinders University*

Background: The difficulty in identifying Autistic Disorder at an early age may partly arise from the fact that existing tools and the current diagnostic criteria defined in the ICD-10 (1992) and DSM-IV-TR (2000) describe behaviors thought to occur later in the developmental pathology of the disorder.
Objectives: The ADEC (Autism Detection in Early Childhood; ACER, 2007) was developed to provide a psychometrically sound screening tool for clinicians to more accurately identify autism in children under the age of three years
Methods: The referred sample ranged in age from

14 to 36 months. Data were collected from three groups; those who had received a diagnosis of Autistic Disorder, those at risk of developing the disorder and typically developing children. The concurrent validity of the tool was examined by administering it together with the Childhood Autism Rating Scale (CARS; Schopler, Reichler, De Vellis, & Daly, 1980), the Autism Diagnostic Interview - Revised (ADI-R) (Le Couteur et al., 1989; Lord, Rutter, & Le Couteur, 1994), DSM-IV-TR (APA, 2000) criteria and Modified Checklist for Autism in Toddlers (M-CHAT). Other psychometric properties relating to its validity and reliability are also addressed.
Results: The ADEC was well-correlated with existing measures of Autistic Disorder some of which are labour intensive and require staff highly trained in the administration and interpretation of these data. Further, when comparing the development of skills in the autism group to that in typically developing group, the age at which the absence of these skills becomes of clinical significance is noted.
and Conclusions: Results indicate the ADEC is effective at detecting Autistic Disorder in young pre-verbal children. Overall these data support previous research suggesting that this tool is an efficient and easily administered assessment tool that can lead to earlier detection and in turn intervention that should enhance the prognosis for the child.

Oral Presentations Program
118 Epidemiology

118.00 Prenatal Exposure to beta$_2$-Adrenergic Receptor Agonists and Risk of Autism Spectrum Disorders. L. Croen*[1], S. L. Connors[2], M. Matevia[1], C. Newschaffer[3] and A. W. Zimmerman[2], (1)*Kaiser Permanente*, (2)*Kennedy Krieger Institute*, (3)*Drexel University School of Public Health*

Background: Abnormal outcomes in brain and tissue function have been reported following prenatal administration of β2-adrenergic receptor (B2AR) agonists in animals. Prenatal exposure to terbutaline, a B2AR agonist, has been previously linked to autism in dizygotic twins, and the prevalence of more active B2AR polymorphisms has been reported to be increased in families with autistic individuals.
Objectives: To investigate the association between maternal exposure to B2AR agonists during pregnancy and risk of delivering an infant subsequently diagnosed with an autism spectrum disorder (ASD).
Methods: We conducted a large case-control study nested within the cohort of infants born from 1995-1999 at northern California Kaiser Permanente (KPNC) hospitals. Cases (n=398) were children with an ASD diagnosis recorded in KPNC outpatient databases; controls (n=410) were children without an ASD diagnosis, randomly sampled and frequency-matched to cases on sex, birth year, and birth hospital. Information on maternal exposure to B2AR agonists and drugs with similar postnatal cell signaling effects after prenatal exposure (mimics) was ascertained from the KPNC pharmacy database, which records all dispensed prescriptions for KPNC members, and abstracted from prenatal medical records using a standardized form. All inpatient and outpatient prescriptions in the 3 months before conception through the end of the pregnancy with the study child were identified.
Results: The frequency of exposure to B2AR agonists or mimics anytime during pregnancy was somewhat higher for the mothers of children with autism (21.4%) compared with the mothers of control children (17.3%), but differences were not statistically significant. After controlling for covariates (birth order, plurality, maternal age, maternal education, and birth weight), the risk of delivering a child later diagnosed with an ASD was over 3 times higher for women with B2AR agonist exposure in the 3 months before conception (OR=3.48, 95% CI 1.2-10.3), and approximately twice as high for women with 1st trimester (OR=1.94, 95% CI 0.87-4.30) or 2nd trimester (OR=2.1, 95% CI 1.0-4.1) exposure. Albuterol was the most frequently used B2AR agonist among mothers of both cases and controls during the preconception period (2.3% vs. 1.2%), as well as in the 1st trimester (3.8% vs. 2.2%) and 2nd trimester (5.3% vs. 3.4%). Frequency of maternal exposure to any B2AR agonist was highest in the 3rd trimester, but did not differ between cases and controls (17.6% vs. 15.6%, P=0.45, OR=1.1, 95% CI 0.71-1.6). Terbutaline accounted for the majority of 3rd trimester exposure in both case and control mothers (10.3% vs. 7.2%, P=0.13, OR=1.34, 95% CI 0.81-2.25).
Conclusions: These results suggest that B2AR agonist exposure in the first half of pregnancy may be associated with an increase in risk of having a child with autism spectrum disorders.

118.01 Maternal Periconceptional Folic Acid Intake and Risk of Autism Spectrum Disorders in the CHARGE Study. R. J. Schmidt*, R. L. Hansen and I. Hertz-Picciotto, *University of California at Davis*

Background: Folic acid supplementation can prevent 50-70 percent of neural tube defects (NTDs) and has been associated with reduced risk of neurological disorders and decreased symptoms in children with autism (AU). Genetic and metabolic differences associated with the folate pathway have also been described for parents and children with autism.

Objectives: To determine whether women who took supplements containing folic acid before and during pregnancy were less likely to deliver children who developed AU, autism spectrum disorders (ASD), or developmental delays (DD) as compared with women not taking supplements during that time period.

Methods: Within the Childhood Autism Risks from Genetics and the Environment (CHARGE) study, cases of AU and ASD were confirmed at the UC Davis M.I.N.D. Institute clinic using the Autism Diagnostic Observation Schedules and the Autism Diagnostic Interview by staff with established reliability. The Mullen's Scales of Early Learning and the Vineland Adaptive Behavior Scales were used to confirm DD in children. Population-based controls were selected by stratified random sampling using birth files and typical development was confirmed based on the above assessments. Intake of prenatal vitamins, multivitamins, folic acid-specific vitamins, other supplements, and cereal was collected through telephone interviews and examined for the three months before and throughout pregnancy and breastfeeding. Daily average total supplemental folic acid was quantified for each mother based on reported dose, brands, and frequency of use for each source. Logistic regression models were fit adjusting for maternal education. We estimated odds ratios (aOR) comparing affected with unaffected children for maternal folic acid intake, along with 95% confidence intervals (CI). Group differences in mean folic acid intake were assessed using Wilcoxon two-sample tests.

Results: Families of 280 TD, 300 AU, 125 ASD, and 108 DD confirmed children participated in the CHARGE study from late 2003 through September 2008. Mean maternal folic acid intake was greater for mothers of TD children than for mothers of AU and ASD children throughout the entire index period, with the greatest difference observed for the month before and the first month of pregnancy (533.7 and 626.8 mcg for mothers of AU/ASD and TD children, respectively, p=0.02). This difference was primarily due to a higher proportion of mothers of TD children consuming prenatal vitamins before and during the first month of pregnancy (aOR=0.43; CI:0.28,0.67). A dose-related trend was observed; women reporting the highest average daily intake of total folic acid during the month before and the first month of pregnancy had the lowest risk of having children diagnosed with AU/ASD (p for trend = 0.01). Mothers of DD children also had lower mean daily folic acid intake (566.2 mcg) relative to mothers of TD children, although the difference was not significant (p=0.23).

Conclusions: Folic acid supplements taken in the periconceptional period may reduce the risk of AU and ASD. The level of supplementation needed is likely influenced by the genetic background of the mother and/or child, particularly for genes within the folate and methylation pathways. Replication of these findings and further investigations of mechanisms involved are warranted.

118.02 Sickle Cell Disease and Autism Spectrum Disorders. A. W. Zimmerman*[1], L. C. Lee[2], J. Baio[3], J. R. Keefer[4], R. S. Kirby[5], C. Newschaffer[6], J. S. Nicholas[7], M. Durkin[8], W. Zahorodny[9] and K. D. Smith[1], (1)*Kennedy Krieger Institute*, (2)*Johns Hopkins Univ. School of Public Health*, (3)*National Center on Birth Defects and Developmental Disabilities*, (4)*Johns Hopkins School of Medicine*, (5)*University of South Florida*, (6)*Drexel University School of Public Health*, (7)*Medical University of South Carolina*, (8)*University of Wisconsin-Madison*, (9)*University of Medicine and Dentistry of New Jersey*

Background: Over 60 known medical disorders have been associated with increased risk of autism spectrum disorders (ASD) but none has been shown to be protective, either genetically or postnatally. Sickle cell disease (SCD) is a common heritable hemoglobinopathy that primarily affects African Americans (AA) with onset during the first year of life and associated with neurological complications, including stroke and cognitive decline, but has not been reported in association with ASD. SCD may provide postnatal physiologic stress that has a cellular protective effect during brain development despite the risk for vascular injury. Clinical improvements during fever in ASD also may result from activation of cellular stress

responses (CSR). Objectives: This study examined the prevalence of SCD in AA with ASD, intellectual disability (ID) and cerebral palsy (CP) compared to the US population. We hypothesized that SCD might decrease the risk or ameliorate ASD severity and therefore the SCD prevalence among children with ASD would be lower than expected. Methods: Data on ASD, ID, and CP were obtained from the Autism and Developmental Disabilities Monitoring (ADDM) Network. ADDM identifies children with ASD, ID, and CP through systematic review of records from multiple educational and health sources. The current analysis utilized data on 8-year-old children from fourteen regions of the US over three surveillance years: 2000, 2002, and 2004. The total number of AA in ADDM included 1216 children with ASD, 1243 with ID, and 241 with CP. Presence of SCD in ADDM was identified by SCD diagnostic billing code or notation of SCD diagnosis in record. Comparison data on SCD in the general population were derived from the US National Newborn Screening Report - 2000, as the total number with SCD among all AA newborns screened nationwide. Results: Four children with SCD were found among 1216 AA with ASD (3.29/1000). SCD observed in the ASD group was not significantly higher than in the general AA population (Relative Risk =1.68; 95% Confidence Limits (CL) =0.63, 4.48). However SCD in CP and ID was 8.49 (95%CL: 3.21, 22.48) and 2.47 (95%CL: 1.11, 5.50) times, respectively, greater than expected. Clinical phenotypes in the 4 AA children with ASD and SCD showed mild cognitive impairment. Conclusions: Compared with the national AA population, SCD in ASD is not significantly more prevalent, whereas SCD in CP and ID is significantly more prevalent. Data from the small number of children in this pilot study do not support our hypothesis of decreased risk of ASD in SCD; however, SCD may ameliorate its cognitive severity. The higher frequency of SCD in children with CP is likely attributable to strokes. Behavioral changes and ID may also occur in some children with SCD due to early cerebrovascular disease. Benefits of CSR may be masked by the presence of vascular damage. Future studies should clarify the severity of SCD and its relationship to autism and protection or neurological injury due to SCD. A very large sample size will be required for sufficient statistical power to define the role of SCD in ASD.

118.03 A Clarification of the Association Between Parental Age and the Risk of Autism. J. F. Shelton*[1], D. J. Tancredi[2] and I. Hertz-Picciotto[3], (1)*University of California, Davis*, (2)*UC Davis School of Medicine and Center for Healthcare Policy and Research*, (3)*University of California at Davis*

Background: Previous reports on the risk of autism among children born to older parents have yielded conflicting results as to how increased paternal/maternal age affects risk.

Objectives: To quantify the association between increasing parental ages and the risk of autism and to evaluate the percent attributable risk due to older average maternal age in California between 1990 and 1999.

Methods: By analyzing restricted subgroups of parental age in a California birth cohort of over 5.6 million children, we were able to clarify the independent effects of parental age in a population large enough to evaluate discordant parental age pairings. Multivariate logistic regression models were adjusted for the other parent's age, maternal and paternal education, maternal and paternal race/ethnicity, year of birth, parity, and insurance payment type. When age effects were modeled categorically, the maternal/ paternal reference age group was 25-29. A variance inflation factor was used to adjust confidence intervals to account for the possibility of repeated births from within the same family.

Results: We observed consistent stepwise increased risk for autism with advancing maternal age across all strata of paternal age. The risk of autism for fathers 30 –34 increased from an OR_a of 0.96 (95% CI 0.76-1.2) among mothers < 25 to 1.92 among mothers 40+ (95% CI 1.31-2.79), a trend consistent across subgroups of paternal age. The increased risk of autism from advancing paternal age was larger for mothers < 30 than among mothers > 30, contributing almost no pattern of increased risk to mothers over 40. Among mothers < 25, fathers <25 had an OR_a of 0.84 (95%CI 0.69-1.01) and fathers 40+ produced the highest OR_a of 1.91 (95% CI 1.32-2.74), increasing monotonically per five-year subgroups of maternal age. Among mothers over 40, paternal age showed a steady trend 30-34 (OR_a =1.39), 35-39 (OR_a =1.34), and 40+ (OR_a =1.31) of slightly elevated risk. Additionally, we calculated the number of expected cases in 1999 if the age distribution of mothers had been the same as 1990, and estimate 3.8% of the observed increase in autism cases in California between 1990 and 1999 can be attributed to the trend

towards older maternal age observed over that time period.

Conclusions: Because maternal and paternal ages are highly correlated, previous analysis on smaller populations have produced mixed results as to which parent contributes the increased risk of autism. Through stratified analysis, we were able to detect heterogeneity of the paternal age effect, decreasing in magnitude as mothers age increased. Effect measure modification of paternal age by maternal age indicates that the maternal age effect overwhelms the paternal age effect among mothers over 30, while increased paternal age contributes a stepwise risk among mothers under 30. We conclude that advanced maternal age increases the risk of autism independent of paternal age, and paternal age increases the risk of autism dependent on the mother's age. Approximately 3.8% of the cases observed in 1999 may be attributable to risk factors associated with older average maternal age between 1990 and 1999.

118.04 Factors Associated with Age of Diagnosis among Medicaid-Enrolled Children with Autism Spectrum Disorders in the United States. D. S. Mandell*[1], K. H. Morales[1], M. Xie[1], D. Polsky[1], A. Stahmer[2] and S. C. Marcus[3], (1)*University of Pennsylvania School of Medicine*, (2)*Rady Children's Hospital*, (3)*University of Pennsylvania School of Social Policy and Practice*

Background: Early diagnosis of autism spectrum disorders (ASD) is critically important, in large part because a growing body of evidence suggests that earlier intervention results in better outcomes. Despite the fact that autistic disorder can be diagnosed reliably by experienced clinicians in children as young as 24 months, studies suggest that the average age of diagnosis often is not until children are between 3 and 6 years of age, and varies as a function of families' socio-demographic characteristics. While prior studies provided important information both on estimates and correlates of age of diagnosis, interpretation is limited because they relied on survey strategies subject to selection bias or were limited to small geographic areas. The current study builds on previous research by using a national dataset and includes information about child characteristics, state policies, and county resources that may affect age of diagnosis.

Objectives: to estimate the association between child, county and state characteristics and age of ASD diagnosis among Medicaid-enrolled children

Methods: Medicaid enrollment and claims data for all 50 US states and the District of Columbia from 2001-04 were linked with county-level data from the Area Resource File and the National Center for Education Statistics, which provided information on education and healthcare resources. The sample included all Medicaid-enrolled children age <9 years who 1) had a Medicaid claim associated with an ASD diagnosis (ICD-10 code 299.xx) between July 1, 2001 December 31, 2004; and 2) did not have any claim associated with an ASD diagnosis in the 6 months prior. Linear regression with random effects was used to estimate the effect of child, county and state characteristics on age of diagnosis.

Results: There were 74,512 Medicaid-enrolled children <9 years of age with a first diagnosis of ASD during the study period. The average age of diagnosis for the entire sample was 5.2 (SD = 1.4) years, was similar for those with an autistic disorder (299.0) diagnosis (5.1, SD = 1.5), and varied considerably by state and by county within states. Ongoing analyses suggest the important contribution of county medical and school resources and state policies that govern funding for autism treatment services.

Conclusions: To our knowledge, this is the first national study of correlates of age of diagnosis among children with ASD. Limitations include concerns about the validity of diagnosis in community settings, the generalizability of the findings to non-Medicaid-enrolled children, and the inability to distinguish between PDD-NOS and Asperger's disorder in our data. Still, Medicaid serves 1 in 4 children in the US; the results suggest that ASD is diagnosed much later than is optimal among these children, and that socio-demographic characteristics as well as local healthcare resources and state policies contribute to disparities in age of diagnosis.

118.05 Factors That Influence Age of Identification of Children with Autism and Pervasive Developmental Disorder-Not Otherwise Specified. C. R. Adelman*[1] and S. U. Peters[2], (1)*University of Houston*, (2)*Baylor College of Medicine*

Background: Early diagnosis of autism spectrum disorders (ASD) is crucial because early

identification can lead to early intervention, which has been shown to improve the outcome of affected children.

Objectives: This study explored the current mean age of diagnosis of Autism and Pervasive Developmental Disorder, NOS in the United States, whether average age of diagnosis of children with Autism and Pervasive Developmental Disorder NOS is declining and whether average age of diagnosis differs in the four regions in the United States. A linear regression analysis was performed to determine which socio-demographic factors, clinical factors and pediatrician practices predict age of diagnosis.

Methods: Potential participants were recruited with the assistance of the Interactive Autism Network (IAN) Research Database at the Kennedy Krieger Institute and Johns Hopkins Medicine in Baltimore, sponsored by the Autism Speaks Foundation. Participants were selected from a pool of participants who have registered with IAN, who have agreed to participate in autism research, and whose children met the study criteria. The potential participants were sent a recruitment letter via email by IAN research personnel, which included a link to the on-line survey. The study description and a link to the survey were also posted on the IAN Community Research Opportunities Bulletin Board.
Results: A sample size of 654 participants was used for data analysis. Current age of diagnosis in months of autistic disorder and PDD-NOS in the United States was 37.78, and SD=16.269. Results of a one-way ANOVA indicated differences in age of diagnosis among the four regions in the United States F (3, 650) = 7.618, p=.01). Tukey's post hoc comparisons of the groups indicated that the mean age of diagnosis in months in the Midwest (M=42.1) was significantly later than in the Northeast (M=35.3, p=.000) and South (M=35.5, p=.000). Results of a Pearson Correlation indicated a significant negative correlation (r=-.409, n=654, p=.000) between date of birth and age of diagnosis, with later birthdays being associated with lower age of diagnosis. Regression results were statistically significant, $F(25, 620)=7.549$, $p<.001$, $R^2=.233$. Having autistic older sibling/s, being referred to ECI, and having a pediatrician who performed an in-depth screening in response to parent concerns, were negatively correlated with the logarithm of age of diagnosis, while having first symptoms of non-autism specific behavioral difficulties, being given a non-ASD diagnosis prior to ASD diagnosis and switching pediatricians during first five years of life, were positively correlated with the logarithm of age of diagnosis.
Conclusions: Although the results of this study demonstrate that average age of diagnosis is still within the range reported almost ten years ago, the results are also promising, as younger children in the study were likely to be diagnosed at younger ages. Results of this study suggest that more targeted efforts need to take place in the Midwest, where age of diagnosis was found to be significantly later than in the Northeast and South regions. This study also identifies some factors associated with age identification of ASD, which may useful when developing programs for early identification of ASD.

119 Innovative Technologies Demonstration Session

Innovative Technologies for Understanding and Supporting Persons with Autism Spectrum Disorders: With kind support from the Autism Speaks' Innovative Technology for Autism (ITA) Initiative, this session will provide live demonstrations of a number of innovative technologies that, alone or in conjunction, can be used beneficially in a number of critical areas affecting individuals with ASD, their families, and professionals who strive to better understand and support them. Recent advancements in the areas of video and audio capture technology; computer architecture, hardware, and software; web-based data collection methods; on-body physical and physiological sensing; robotics; virtual reality; and more will be presented, illustrating how this technology can enhance and accelerate the pace of autism research and treatment by providing broader access to professional resources; reducing treatment costs; promoting interventions that increase generalizability of learned skills; and furthering research recruitment, implementation, and data collection and analysis.

119.00 T0 iSocial: a 3D-Virtual Learning Environment for Enhanced Social Interaction and Development of Social Competence. J. Stichter*[1], C. Schmidt[1] and M. Schmidt[2], (1)*Thompson Center for Autism and Neurodevelopmental Disabilities*, (2)*University of Missouri*

Background:
iSocial is a multi-user collaborative three-dimensional virtual learning environment (3D-VLE) intended to engage youth with ASD in curriculum activities that target the remediation of core deficits in social functioning. 3D-VLEs have the potential to add social and physical attributes to traditional computer-supported learning, provide anytime and anywhere content delivery,

allow for feedback, can adapt to users' needs, and can record behavior for diagnosis and assessment. Prior research has shown that individuals with ASD can use and interpret VLEs successfully and use VLEs to learn simple social skills (Cobb et al., 2002; Mitchell, Parsons, & Leonard, 2007). However, prior work focused on single users practicing limited skill sets taught in isolation of other skills. By adapting and implementing in a 3D-VLE, a curriculum with demonstrated impact for improving social competence when implemented in a face-to-face small group setting (Stichter, et al., 2007), iSocial seeks to immerse youth in a multi-user VLE for multiple and integrated experiences so they may learn collaboratively with and from others.

Objectives:

A field test of a single unit from the social competence curriculum was undertaken during the Fall of 2008 at the University of Missouri's Thompson Center for Autism and Neurodevelopmental Disorders. Two separate groups participated in six virtual lessons, each consisting of two youths (males on the autism spectrum, ages 11-14), an online guide, as well as a technical "helper" in the VLE, and a facilitator for each youth. In adherence to design research for system development, the key purposes of this initial field test were to (1) assess the efficacy of design decisions for adapting the face-to-face based curriculum into the new medium, (2) identify issues with system usage and (3) generate a trajectory for system improvement.

Methods:

Data collected during the field test consisted of a technology competency survey administered at the beginning of the study, social presence surveys, adapted from Bailenson, Beal et al. (2001), administered at the end of each session, screen and audio recordings of all participants' sessions within the VLE and videotaped recordings of participants with their facilitators physically using computers for each session. Video data were analyzed utilizing an all-views qualitative analysis (AVQA) technique in which all participants' virtual and real-world videos can be viewed and coded synchronously.

Results:

Preliminary results fall into four categories: (1) challenges of adapting a face-to-face curriculum into 3D-VLE medium, (2) challenges of enabling and shaping appropriate social interaction within the medium, (3) easing transitions and reducing distractions and (4) leveraging the engagement and enthusiasm of youth for being a part of iSocial toward achieving desired learning outcomes. Participants found iSocial to be easy to use, enjoyed their experience in the iSocial field test and engaged in pro-social behavior.

Conclusions:

The preliminary results provide numerous points of departure for further design, development and research into utilization of 3D-VLE technologies for facilitation of collaborative virtual social competence instruction for individuals with ASD.

119.01 T1 Analysis of Automatically Generated Usage Data on 1,100 Children Using the TeachTown Basics Computer-Assisted Intervention Program. C. Whalen*[1], M. Vaupel[1], S. Cernich[1], K. MacDonald[1], P. Fielding[2] and E. Dashen[1], (1)*Jigsaw Learning*, (2)*Independent Consultant*

Background: Computer-Assisted Instruction (CAI) has increased substantially in popularity due to the increasing prevalence of ASD and shortages in available services. There is also a growing body of research in this area looking at the efficacy and potential of CAI. TeachTown Basics is a program that teaches language, social skills, life skills, academic and cognitive skills (4 domains) through an ABA-based computer program. The program includes computer learning for the child along with automatic data collection. A system for keeping session notes and communicating among the child's team is also included, as well as over 100 off-computer generalization activities for working on skills in the natural environment. Objectives: The purpose of this study was to pilot the effectiveness, as well as common uses of the software, with 1,100 children. Methods: Automatic data has been collected on more than 1000 children to date (more may be presented at conference) using the TeachTown Basics software over the past 3 years. Children were selected who demonstrated at least 3 months of regular use (minimum of 1 hour/week on average over at least 3 months). Average scores on pre and post tests were analyzed, along with an analysis of the frequency of use, usage patterns (e.g. number and frequency of notes entered, average session length, etc.). Results: Significant changes from pre to post tests were shown for all 4 learning domains, average session time was 15 minutes, average use was 6 times/week, children had average of 1.5 facilitators, average age of user was 6 years old (range 2-21 years), average notes use was 3 per week. This, and other usage data will be presented. Conclusions: Initial results show promise for the use of this program to teach

children with ASD and track their progress remotely. The computer intervention program will be demonstrated, along with a glimpse at the tools used for creating the program and collecting the data. Future directions for behavioral interventions implementing technology will be discussed and pilot data from a clinical trial currently in progress in a large public school will be presented.

119.02 T2 Museum Hunt: a Computerized Eye-Tracking Game. F. Hurewitz*, M. Brennan, E. Boucher and F. Lee, *Drexel University*

Background: There has been increasing interest in the creation of technology based interventions to facilitate learning of social skills such as facial recognition in individuals with autism. One lack in current programs is that they usually involve static faces, and they measure the user's ability to attend to the relevant information via explicit response (key presses) in lieu of the on-line abilities required to navigate real social interactions. A further limitation is that programs requiring rote memorization can be seen as boring by the user, and may not be reinforcing enough for longterm use.

Objectives: We present as a "proof of concept" a demonstration of an interactive video game designed to assist individuals with autism in learning reciprocal social skills such as gaze following, social referencing, and attention to facial expressions and facial configurations. This game uniquely uses eyetracking technology (implemented on a TOBII T60 eyetracker) to assess if users are attending in real time to relevant aspects of the virtual world. Based on the users eyegaze, the game increases or decreases the number and explicitness of social/attentional cues. Furthermore, eyetracking data is used to determine if the software based intervention increases the automaticity in which the game user notices these cues.

Methods: The game, Museum Hunt, is comprised of a series of expandable and reconfigurable scenarios which encourage children to solve a mystery by assisting an avatar detective. The detective (and the computer user) must use active cues that occur in the course of a real time adventure to solve the mystery. Activities include matching mug shots to faces of avatars that passed by carrying a purloined object, following the gaze of a crowd of people to find out where the thief is hiding, or determining emotion/facial expression of an avatar. Difficulty levels can be adjusted (e.g. to make the mugshot task more difficult, it may use a disguised individual who has dyed hair and glasses.) By creating this interaction in a gaming format, we create a fun and reinforcing format to teach social skills. Additionally, the game has procedurally generated stories and activity sets which give the player new experiences each time they play. It is developed in flash and has a mode without eye tracking which allows it to run on any standard web browser.

Results: Our presentation will include a demonstration of the eyetracking paradigm, and discussion of the prospects for expanding this technology to new scenarios, including contingent eyegaze interactions with avatars.

Conclusions: We demonstrate the feasibility of creating fun, usable and dynamic software-based interventions for individuals with autism to practice social skills. We also for the first time establish that monitor-embedded eyetrackers can be used as input devices for avatar based gaming. As eyetracking technology becomes more accessible in terms of cost and usability, this is a promising medium for delivering interventions that train individuals to modulate attention and the social use of eyegaze.

119.03 T3 DeePAD: a Deep Pressure Touch Application Device Using Pneumatic Pressure. B. Mullen* and S. Krishnamurty, *University of Massachusetts-Amherst*

Background: Sensory Integration (SI) is among the top five most commonly used therapies to help children with autism cope in everyday situations. It has been observed by therapists and teachers that providing SI to children with autism can result in positive outcomes, including a reduction in self-injurious behaviors, an increase of on task behavior (attention), and a reduction in anxiety. A widely used SI therapy is the application of a tactile stimulus known as Deep Pressure Touch Stimulation (DPTS) - firm pressure like a firm hug, swaddling, or firm petting. Currently, DPTS is often applied using weighted or elastic garments and used in controlled environments, such as in schools and hospitals. Current application methods are passive systems that provide limited control over the amount of pressure applied and customization. Furthermore, there is a lack of literature on requirements, safety and efficacy of DPTS products.

Objectives: To develop an assistive sensory

device that is universally designed, humane, person-centered, and evidence-based that leads to improved quality of life for children with autism. The resulting device must be able to successfully go from bench-top to bedside and back by being adoptable and commercially viable.
Methods: We have designed and developed a novel pneumatic **D**eep **P**ressure touch **A**pplication **D**evice (**DeePAD)**. To achieve our objectives, we have adopted a bench-top to bedside and back design approach focusing on function, validation, adoptability, and commercialization. To test function, we tested the device with normal adults to evaluate its effectiveness in providing a custom fit compared to the gold standard weighted vests. For validation purposes, we conducted bench top tests to collect and calibrate in situ pressure data. To test its adoptability, we interviewed parents, teachers, and therapists. To test its commercial viability, we developed a comprehensive business plan.
Results: The device was able to easily adjust to fit many different body types. Bench-top tests have shown that the product can measure and deliver a continuous scale of pressure in situ. Interview participants have responded positively to the innovative features of **DeePAD**. Our business plan won the 2008 UMass Technology Innovation Competition and we have received numerous non-solicited requests to purchase our product.
Conclusions: We will demonstrate **DeePAD**, the first deep pressure product that has been designed for function, validation, adoption and commercialization, thus ensuring a quick transition from bench-top to bedside and back. The device offers children with autism a person-centered sensory device that can be customized to their sensory needs, while providing caregivers an easy to use tool that can enable every customer a unique and customized sensory experience. More importantly, the versatility of this device, with its on-board pressure data collection abilities, allows researchers the ability and control to rigorously study the efficacy of deep pressure touch in a multitude of clinical and therapeutic settings, as well as in real world use. In collaboration with the UMass Center for Language, Speech, and Hearing (CLSH), we are currently testing **DeePAD**'s efficacy by measuring participant's motor, behavioral, speech and language outcomes during therapy sessions.

119.04 T4 Automated Detection of Stereotypical Motor Movements.

M. S. Goodwin*[1], S. S. Intille[1], F. Albinali[1], W. F. Velicer[2] and J. Groden[3], (1)*Massachusetts Institute of Technology*, (2)*University of Rhode Island*, (3)*The Groden Center, Inc.*

Background: Stereotypical motor movements can be one of the most disruptive types of behavior seen in persons on the autism spectrum. Engagement in these behaviors can lead to social stigmatization and complicate social interaction. Moreover, if stereotypical motor movements become dominant in an individual's behavioral repertoire, they can interfere with the performance of established skills and acquisition of new skills, and may lead to self-injurious behavior. Unfortunately, a lack of accurate and timely measures has made it difficult to determine what function(s) stereotypical motor movements serve and whether interventions aimed at reducing, replacing, or preventing them are effective.

Objectives: Utilize sensor technology to provide a measure of stereotypical motor movements that may be more objective, detailed, and precise than rating scales and direct observation, and more time-efficient than video-based methods. Use of wireless accelerometers and pattern recognition software to automatically detect stereotypical motor movements will be demonstrated and experimental data validating this innovative application of technology will be presented.

Methods: Six participants on the autism spectrum who engaged in stereotypical hand flapping and body rocking were observed repeatedly in both laboratory and classroom settings (for a total of 11 hours) while wearing three small, unobtrusive wireless and wearable movement sensors placed on the left wrist, right wrist, and torso. A digital camera recorded each session. The camera was connected to a computer that synchronized saved video with accelerometer data streams. Start time, end time, and type of stereotypical motor movement were coded both in real-time and offline by two independent raters using custom video coding software. Real-time human coding and computerized pattern recognition performance was compared to offline, "ground truth" video annotations (average inter-rater reliability across offline codes was .95).

Results: In addition to excellent compliance and performance with the sensors across participants and settings, findings revealed that, on average, real-time human coding was correct only 60% of the time across participants in the laboratory and

classroom, while computerized pattern recognition algorithms (C4.5 classifier using five acceleration time and frequency domain features as input) correctly identified (verified with 10-fold cross validation) approximately 90% of stereotypical motor movements observed across participants in the laboratory and approximately 85% observed across participants in the classroom.

Conclusions: The technology-assisted assessment strategy developed in this work has significant clinical implications. First, reliable recording of stereotypical motor movements could enable researchers to study what functional relations may exist between stereotypical motor movements and specific antecedents and consequences. These relations may arise differentially in various environmental settings, in the presence of demand tasks, or in the presence of physiological influences. Second, wireless devices that record stereotypical motor movements could enable teachers, therapists, and caregivers to monitor movement behavior and gather data that can assist with treatment decisions. Finally, documentation of stereotypical motor movements before and after an experimental treatment could facilitate efficacy studies of behavioral and pharmacologic interventions intended to decrease the incidence or severity of stereotypical motor movements.

119.05 T5 Use of a Wearable Recording Device in Therapeutic Interventions for Children with Autism. G. Marcu*, D. H. Nguyen and G. R. Hayes, *University of California, Irvine*

Background: A common problem for caregivers of children with autism is facilitating communication, especially when the children are non-verbal. Caregivers use social stories and references to a child's activities to encourage discussion, but these efforts are challenging and not always effective. Additionally, caregivers are challenged with trying to understand a child's behavior and reactions without the aid of verbal expression from the child. This project applies the use of SenseCam to therapeutic interventions for children with autism.

SenseCam is a small wearable camera developed at Microsoft Research. It takes photographs automatically at a frequency determined either by a preset interval or in response to sensory input. Photographs can be transfered to a computer and watched at different speeds. SenseCam was designed to augment human memory by providing a first-person account of the wearer's activities.

Objectives: In this work, we hypothesized that the use of SenseCam by children with autism will enable greater awareness of the child's perspective during the day and potentially be used in new therapeutic interventions to support communication and understanding. The photographs are captured from the child's perspective, allowing caregivers to review captured events with a child and encourage them to discuss activities and people appearing in these photographs. The primary objective of this work is to develop processes for inclusion of SenseCam technology into everyday use by children with autism and to modify interfaces to SenseCam media for use in these interventions.

Methods: Children with autism, their daily activities, and their social interactions were observed in the classroom. Interviews with teachers and parents of children with autism provided additional data about communication challenges. Interviews with autism specialists informed the design of use of SenseCam by children with autism.

Results: We have developed a therapeutic intervention using a novel technology--SenseCam from Microsoft Research. In this intervention, children with autism can wear SenseCam during all or part of a typical day. Parents and other caregivers can review photographs taken during school hours while teachers and other school staff review photographs taken during after-school hours. These review sessions can facilitate mutual understanding of activities in these environments and better communication between school and home. Parents, teachers, and other caregivers can also review photographs together with the children to facilitate communication. The photographs can be used to encourage the children to discuss activities, people, social situations, and their feelings. This intervention can improve the children's expression and augment their understanding of social interactions through open discussion about the photographs.

Conclusions: Working in collaboration with schools and autism specialists, we have developed a technology based therapeutic intervention which can enhance caregiver awareness and improve children's communication and social understanding. Future work will involve the deployment and evaluation of SenseCam in the classroom and the home among children with

autism, their parents, teachers, and other caregivers.

119.06 T6 PDA Technology to Improve Self-Awareness in Teens with ASD. D. S. McLeod* and D. A. Lucci, *Massachusetts General Hospital*

Background: It is well documented that individuals with Autism Spectrum Disorders (ASD) and Nonverbal Learning Disabilities (NLD) demonstrate difficulties in social skills and in social awareness. They have difficulty in accurately reporting own feeling and sensory states. They also have challenges in taking perspective on these skills. Successful efforts to address these concerns would likely lead to more successful social interactions and self-management of emotions and sensory states.

Objectives: To demonstrate the effectiveness of PDA technology in increasing self-awareness in Teens with ASD.

Methods: 11 adolescent males: 3 diagnosed with PDD-NOS, 4 Asperger Syndrome, 4 NLD; ages 13 – 17 years old, each had average to above average IQs on the WISC-IV. Each participant was enrolled in a therapeutic summer program. They were assigned in one of two groups that were divided by interest, level of functioning and age. Boys were admitted to camp through an interview and submission of the following documents: school records, psychological reports and completion of agency's own social checklist and the Walker-McConnell Scale of Social Competence and School Adjustment.

Each boy was given a 41 page Instructional Manual that described the usage of the PDA and definitions of the intervention vocabulary. The manual was reviewed during social competency groups led by senior staff. Campers were allowed to bring the Instructional Manual home to review with their parents.

Data was concurrently entered by staff and camper on the staff's PDA and was collected across 4 Contexts (Morning, Mid-Morning, After-Lunch and End of Day) and during 4 Settings (Start of Day, Social Thinking, After Lunch and End of Day). Each Setting had its own set of data collection screens. Data was transferred to a computer and available for charting/graphing. Individual graphical reports were analyzed regularly with the teens to discuss their ratings. The full data set was used to perform statistical analyses.

Results: PDA technology did increase self-awareness in Teens with ASD on several dimensions. Teens using their prior knowledge of conversational partner correlated with improve conversational flow. Teens who talked about their conversational partner's interests correlated positively with partner being more engaged. There is a strong positive correlation between the Teen's perception of being positively engaged and his perception of being helpful to the success of the group. There also is a strong positive correlation between the staff's perception of the Teen's being positively engaged and the Staff's perception of the Teen's being helpful to the success of the group.

Conclusions: PDA technology and visual graphs facilitate participation and interest of teens with ASD in discussing social awareness. It enhances teens' self-awareness of feeling states, sensory systems and cognitive flexibility as it relates to others. PDAs enable discussion about the ASD perspective in comparison to others' perspectives of them. Our data suggests that teens can use the visual graphs to describe their internal states and broaden others' perspectives of individuals with ASD. The poster will include examples of screens and data charts.

119.07 T7 National Database for Autism Research (NDAR): Accelerating Scientific Discovery through Collaborative Bioinformatics. M. F. Huerta*, G. Navidi and D. Hall, *National Institute of Mental Health, National Institutes of Health*

Background:

As autism spectrum disorder (ASD) research increasingly uses computation, informatics, and information technologies, the need for shared conventions and standards has become increasingly obvious and urgent. The use of such common approaches (e.g., including common data formats, vocabularies, ontologies, etc.) is necessary in order for digital data, tools, and resources to work together. When data, tools, and resources can work together, tremendous value is added to the entire research enterprise. And, when common approaches are developed not only for a research community, but by that research community, the chances are good that those conventions and standards will be broadly adopted, and that value will be added to that community's research efforts.

Objectives:

The National Database for Autism Research (NDAR) is the National Institutes of Health's (NIH) response to help organize the research community through a bioinformatics platform, helping the community accelerate scientific discovery by: 1) promoting data sharing, 2) helping organize community based solutions that address community based needs and 3) enabling an investigator to effectively communicate detailed research results.

Methods:

NDAR is a collaborative effort with the ASD research community, for which NDAR is designed to serve, and is the result of formal feedback from many research investigators. NDAR is built on the Biomedical Informatics Research Network (BIRN) platform which allows federation with digital tools and data in other research communities, and promotes collaborative research. NDAR is now accepting submission of over 10,000 discrete variables such as common clinical data (e.g. ADI-R, ADOS, etc.), imaging data in a variety of formats, and genomics data including raw, processed, and results data. Data are accepted based upon defined submission schedules relevant to the research ensuring that data are shared at the appropriate times. In 2008, NDAR received initial data submissions from the NIH Autism Centers of Excellence (ACE) grantees. Other researchers are encouraged to participate in 2009.

Results:

NDAR provides an infrastructure to store, search across, and analyze various types of data while also providing longitudinal storage of a research participant's anonymized information generated by one or more research studies. This allows a researcher to associate a single research participant's anonymized genetic, imaging, clinical assessment and other information even if the data were collected at different locations or through different studies. Based upon community feedback, NDAR is defining a community-based common data dictionary to be extended and enhanced by the research field. Data submission statistics will be shared at IMFAR.

Conclusions:

NDAR facilitates the formation of a world-wide network of autism researchers, regardless of funding source, by harmonizing data, research tools, and institutions so that autism researchers can collaborate in new and productive ways. By doing so, NDAR gives researchers access to more data than they can collect on their own and provides robust tools to analyze the information, making it easier and faster for researchers to gather, evaluate, and share autism research information from a variety of sources, regardless of where that data may reside.

119.08 T8 Demonstration of a Collaborative Interface to Promote Positive Social Interaction Skills by High and Low Functioning Children with Autistic Spectrum Disorder (ASD). M. Zancanaro[1], A. Battocchi*[2], N. Bauminger[3], E. Gal[4], A. Ben-Sasson[4], F. Pianesi[2], D. Tomasini[1] and P. L. Weiss[4], (1)*Bruno Kessler Foundation*, (2)*Fondazione Bruno Kessler*, (3)*Bar-Ilan University*, (4)*University of Haifa*

Background: While various Computer Assisted Instruction tools have resulted in mainly positive effects on children with ASD, responses from both professionals and parents have been mixed; along with the obvious advantage of using such environments with children with ASD, there are those who fear that such tools will increase social withdrawal and encourage compulsive behaviors. However, computer based interventions and virtual environments appear to offer a useful tool for social skills training in children with ASD. Objectives: To demonstrate a new paradigm using a co-located setting that employs the Diamond Touch table originally prototyped by the Mitsubishi Electronic Research Laboratory and now commercialized by CircleTwelve Inc.

Methods: The DiamondTouch has a 32-inch diagonal surface that can be placed flat on a standard table. The graphical user interface is projected onto this surface. It contains an array of antennas embedded in the touch surface. Each antenna transmits a unique signal. Each user has a separate receiver, connected to the user, typically through the user's chair. When a user touches the surface, antennas near the touch point couple an extremely small amount of signal through the user's body and to the receiver. In this way DiamondTouch can distinguish who is touching and distinguish between simultaneous inputs from multiple users. This unique characteristic enables the implementation of cooperative gestures where the system interprets the gestures of more than one user as contributing to a single, combined command

increasing participation and sense of cohesion. Results: Initially, we developed the StoryTable application, whereby pairs of children could interact to construct a common story. In this application we investigated a specific case of cooperative gestures, named "Enforced collaboration", that require that actions on digital objects (e.g., touch, drag) be carried out by two or more users simultaneously. Preliminary investigation with dyads of children with high functioning autism has shown that forcing the simultaneous execution of selected tasks may foster the recognition of the presence of the other, stimulate social behavior (increased eye contact, emotion sharing, and enhanced interest toward the partner), and improve social skills. More recently, we have shown a second interface, the Collaborative Puzzle Game (CPG), to be a feasible tool for lower functioning children with ASD since it does not require the use of language. The Collaborative Puzzle resembles a traditional jigsaw puzzle (an activity that primarily involves visuo-spatial skills). While in the Free Play Condition, players can move puzzle pieces individually, in the Joint Play Condition the Enforced collaboration is active and the puzzle pieces can be moved to the solution area only be means of a joint drag-and-drop action. In an initial study both children with typical development and those with ASD enjoyed using the game and were readily able to learn and execute the various functions of the game within one session with minimal explanations. An increase in collaboration as the sessions progressed for both typical children and those with ASD was observed.

Conclusions: Our tentative conclusion is that the CPG encourages children to interact, whether they have ASD or not.

119.09 T9 Treating Speech Impairments in Autism with Delayed and Rewarding Feedback: Preliminary Investigation. Y. Bonneh*[1], O. Dean-Pardo[2] and J. F. Houde[3], (1)*University of Haifa*, (2)*, (3)*University of California, San Francisco*

Background: Speech impairments are very common in autism and many children with severe autism speak unintelligibly or are even mute. Preliminary investigation of few rare cases, who can nevertheless communicate, revealed that at least some of them have difficulty hearing themselves when attempting to speak intentionally. Based on these observations, on the evidence for a tight link between auditory reception and production via auditory feedback in the normally developing brain and on the extensive evidence for abnormal auditory processing in autism, we hypothesize that speech impairments in autism could be at least in part due to abnormal processing of sensory feedback, which is critical for proper development of speech.

Objectives: Investigate and apply altered auditory and visual feedback methods for training a small number of autistic children with unintelligible speech, for which current therapies are not sufficiently effective.

Methods: Two types of feedback were developed: (1) delayed and amplified echo of the speech and (2) visual feedback as an alternative method to reward successful production. The visual feedback was a movie clip, specifically attractive to the child which was activated with speech production. These methods were applied in a clinical setup of a private speech therapy clinic.

Results: Preliminary application of the approach showed significant improvement in verbal production for two young children (ages 3.5, 4.5) with severe autism and severe speech impairment. In addition, it encouraged and motivated the children to produce speech and improve their cooperation with the therapist. The method was also applied successfully to three non-autistic children with severe developmental verbal dyspraxia. One child (age 6) made frequent phonological errors but could not hear these errors during production. We found that he could easily detect the errors when separated in time (2s delayed feedback) and tended to immediately correct himself following the echo. Similar observations were made with two 3-years old children for whom training with the delayed feedback produced significant improvement. These results and observations are only preliminary and should further be investigated.

Conclusions: Development of an altered feedback speech therapy shows a potential and should be further developed and investigated. Future goals include the development of various feedback enhancements that should direct the speaker towards the desired articulation. If successful, this innovative method would be beneficial for many children with severe autism who are currently unable to speak intelligibly and for which there is no effective therapy.

119.10 T10 Adaptive Robotic Techniques in Children with Autism: Strategies for Utilizing Physiological Data to Optimize Engagement during Computer-Based Interactions. K. C. Welch*, Z. Warren, C. Liu, N. Sarkar and W. Stone, *Vanderbilt University*

Background:

While it is well documented that Autism Spectrum Disorders (ASD) are characterized by impairments in social interaction and communication, questions remain about the neurobiological mechanisms and physiological processes underlying these core-defining behaviors. Recent technological advances have shown initial promise in identifying physiological components associated with social information processing in specific contexts. Despite advances, researchers have not yet successfully developed systems for mapping physiological response systems that can be flexibly applied in real time and real world circumstances.

Objectives:

In the present study, we attempted to develop and apply an adaptive response technology that identified and flexibly modified components of computer-based interactions to optimize engagement in a sample of children with ASD.

Methods:

Six children with autism (ages 13-16 years) and a PPVT-III score of 80 or above participated in six sessions of computer tasks – three solving anagrams and three playing Pong – followed by two sessions of robot-based basketball. A child was involved in the computer tasks while his/her physiological data (i.e., cardiovascular (ECG), electrodermal (EDA), and electromyographic (EMG) signals) were acquired via wearable biofeedback sensors. Changes in task difficulty were designed to evoke varying intensities of three target affective states: liking, engagement, and anxiety. An observing therapist and parent of the participant provided subjective reports during the tasks. Each task session was subdivided into a series of discrete trials, termed epochs. After each epoch subjective reports were collected from the child, his/her parent, and the observing therapist on the child's level (high/low) of the three target affective states during the previous epoch. Physiological data and subjective reports collected during the human-computer interaction tasks were used to train an individualized psychophysiological model. A machine-learning technique, Support Vector Machines, was used to build psychophysiological models, which map between the physiological features and ratings of engagement/affective state. We then evaluated models of interaction where the robot selected its behavior randomly and where the robot autonomously selected its behavior based on the child's current physiological information and predictions derived from their own unique individual psychophysiological model.

Results:

From the closed-loop tasks, we found a robot could maintain and possibly increase subjective ratings of liking during autonomous, real-time interaction with a child with ASD relative to random selection. Prediction accuracies from the psychophysiological models improved with additional physiological information with EMG signals being less discriminatory than ECG and EDA signals.

Conclusions:

Pilot data support the use of psychophysiological modeling as a viable technique for further exploration and incorporation into intervention and interactive experiences for children with ASD. Work incorporating adaptive physiological monitoring into virtual reality platforms aimed at exploring specific social communication and sensory vulnerabilities of children with ASD is underway.

119.11 T11 Revising Reciprocity: Technology Tools for Creating Social Interactions. A. Tartaro* and J. Cassell, *Northwestern University*

Background: The difficulties children with high-functioning autism (HFA) have engaging in reciprocal social interactions with their peers affect relationships, education, and employment opportunities. Reciprocal social interactions rely on *contingency* – maintaining a conversation such that what one says follows from what was previously said – to manage the topic of conversation and engage the other person. Previous studies suggest that children with HFA are less likely to be contingent compared to other children. We propose technology tools as a scaffold for the development of contingency and reciprocity skills.

Objectives: Develop technology tools that allow children with autism to plan, engage in, observe, and revise social interactions. Examine contingency of the social interactions across revisions.

Methods: Design-based research study that used iterative design sessions with individual children to develop tools for planning, engaging in, observing, and revising social interactions. Seven children with high-functioning autism (1 girl), ages 8-12 participated. Severity of autistic social impairment was assessed using the Social Responsiveness Scale (SRS); T-scores were all clinically significant and ranged from mild/moderate to severe. Expressive and receptive language ability was assessed using the Peabody Picture Vocabulary Test (PPVT-4) and the Expressive Vocabulary Test (EVT-2); age equivalents of language ability ranged from 6:2 to 15:9. All participants were enrolled in social groups at a local autism clinical program.

Results: We modified our virtual peer to be authorable, and to function in three modes: collaborate, operate and author, and this study provides evidence of children's use of contingency with the authorable virtual peer. For the collaborate mode, we adapted the "Create a Story" press from the ADOS as a collaborative narrative task where the child and virtual peer work together to tell a story using five objects. This task was developed to (1) be age appropriate; (2) require turn-taking as well as obtaining and incorporating peer input; and (3) use physical objects to enable embodied play to create a connection between the child's physical world and the virtual world of the virtual peer. In operate mode, the child uses an interface to select pre-recorded and animated utterances for the virtual peer while it collaborates on the same task with another person. In author mode, children create new utterances for the virtual peer and design their own interface for operating the virtual peer. Evidence from the design study suggests Authorable Virtual Peers can: (1) be used to identify behaviors that may be affecting reciprocity; (2) provide a scaffold which allows children to employ contingency skills related to reciprocity that are difficult for them in conversation with other children, including: adding new information, asking questions, listening, and providing feedback; and (3) enables children to monitor and modify social behavior.

Conclusions: This technology demo will demonstrate how tools for authoring and operating virtual peers enable children to employ contingency skills related to reciprocity while controlling, monitoring and modifying the social behavior of a virtual peer. We will also demonstrate how the system can be adapted to support different abilities.

119.12 T12 Automatic Retrieval of Mother-Infant Social Games from Unstructured Videos. P. Wang*, J. M. Rehg, G. D. Abowd and R. I. Arriaga, *Georgia Institute of Technology*

Background: Social games are an important source of diagnostic information on social deficiency for autism. Social interaction gestures (most of which arise in the hand movements of social games) are analyzed in recorded videos (retrospective study) or under in-situ observations. Current approach on video editing and behavior coding for retrospective study involves manual scene tagging and selection, and manual behavior scoring with trained professionals. It leads to highly inefficient use of both human time and videos, and subjectivity and inconsistency in coding results. Our long term goal is to facilitate the process by developing techniques to automate video filtering and behavior coding.

Objectives: Develop methods for automatically retrieving social games from unstructured videos.

Methods: Our computational model characterizes social games as **quasi-periodic spatio-temporal patterns** based on its four attributes: *dyadic, interactive, multi-instantiation and repetitive*. Social games are fundamentally dyadic interactions, and the correspondent motion patterns are temporally-interacting and spatially-distinct. The game itself is loosely defined by an abstract game rule, which enables multiple game instantiations. Finally the repetition (with a permissible range of variations) will generate approximately same categorical motion patterns throughout a game instantiation. From the retrieval perspective, the quasi-periodic spatio-temporal pattern should distinguish social games from other non-game footages. Our strategy takes three steps. First, we process the footage to identify segments that are recorded with a relatively static camera. We assume the videographer tries to hold the camcorder still when recording a social game. Second, we use a temporal data mining technique called InfoMiner (Yang et. al., 2001) to find the quasi-periodic

patterns from the filtered video. The entire videos are divided into short segments (400 to 600 frame-long on average). Then a sequence of motion symbols is extracted from each segment. For each sequence, InfoMiner finds the sequential patterns that exhibit a repetitive structure in that sequence. Finally, we will use validation method that integrates the spatial and temporal relationships to examine the hypothetical patterns.

Results: Our testing sequence contains 208 video segments, with 53 games (14 patty-cake and 39 ball games) and 155 non-game activities (such as single person play with toy, two-person conversations). Retrieval performance is evaluated by recall and precision. Exhaustive manual search has 100% recall (all the games are found) and 25.5% precision (53/208, which means 74.5% time are wasted at navigating non-game videos). Our method returns 92.45% recall and 31% precision. It doesn't require any human-preprocessing once the video is ripped from DV or VHS tapes. It takes only seconds to decide which segment contains social games after the motion symbols are extracted. The reported results are obtained from the first two steps. Currently the validation stage for our retrieval system is still under development. We believe that validation will eliminate many false positives and retrieval precision will be much improved.

Conclusions: The social game retrieval system has shown promising performance compared to manual retrieval and is the first step towards automatic retrieval of general social interactions.

119.13 T13 FaceSay - Social Skills Games That Work. C. Wimsatt*, *Symbionica, LLC*

Background: A big challenge for children and adults on the spectrum, as well as educators and providers, is generalizing Social Skills to everyday life. FaceSay is one of the first, and as far as we know, the only technology intervention to show generalization to the playground in a randomized controlled study (N=49, at the University of Alabama, Birmingham, publication in preparation). Because FaceSay is scaleable - relatively low cost, little or no training, accessible as a download, can be used independently by higher functioning students, complementary to other interventions - it has the potential to provide a large benefit.

Objectives: The overal goal was to determine if a computer-based social skills intervention for children with autism or Asperger Syndrome is effective in improving specific social skills. The specific aims of the study were to investigate the effects of an avatar assistant on the emotional cognition of children with an ASD's emotional. The study also examined the social skills effects of the intervention.

Methods: Forty-nine children with autism or Asperger Syndrome participated in the project.The children had previously received a diagnosis of autism (n=25) or Asperger Syndrome (n=24) according to the criteria specified by the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association, 1994). The children were recruited from several sources, including the Autism Society of Alabama, Glenwood Inc, Mitchell's Place, and local elementary schools.

The children were randomly assigned to the training group (FaceSay) or the control group (Tux Paint Software). All children were asked to attend two 2 sessions per week (10-25 minutes each) for a total of 12 sessions. Children who attended greater than 83% of the sessions were included in the analyses

Results:

FaceSay Intervention Groups --
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Conclusions: While all of the results are encouraging, the generalization is the most encouraging and the biggest surprise. Based on results from other strong projects, the researchers expected that no generalization would be found. Additional research is underway to try to replicate and better measure the generalization. One of the biggest challenges in measuring generalization is how to make a controlled measure of an uncontrolled interaction? We are exploring the use of LifeShirts, as well as new equipment from SeeingMachines and software from Michael Spezio to automatically measure

dwell time, eye vs mouth in naturalistic interactions between teacher and student. In addition, a study with neurotypical preschool children using FaceSay has shown promise for using FaceSay inclusively and "prophylactically". One recent development is the exploration by Sally Roger's team that attention to faces may play a role not just in emotion recognition, but in imitation.

119.14 T14 A Touch-Screen Smarphone Application and An Online Community for the Improvement of the Communication of Children with Severe Autism and for the Support of Their Teachers and Therapists. G. De Leo*[1], C. Gonzales[2], P. Battagiri[1] and G. Leroy[2], (1)*Old Dominion University*, (2)*Claremont Graduate University*

Background: The growth rate of children diagnosed with autism is enormous. From 1992 to 2003, there was an 805% cumulative growth rate, and in 2003, 1 out of 264 children were diagnosed with autism. Approximately one-third to one-half of individuals with autism is not able to communicate their daily needs. To help children with severe autism communicate, the paper-based Picture Exchange Communication System (PECS) is commonly used. However, the intrinsic difficulties associated with the use of PECS (such as the time needed to create a new laminated picture and to build a sentence) make communication between children with autism and their caregivers hard to achieve. Moreover, teachers and therapists of children with autism do not have access to any centralized repository where they can access relevant, up-to-date information on teaching approaches, share copyright-free images, discuss their teaching styles, and find help for evaluating the progress of the children.

Objectives: The objectives of this research project were to create: 1) an open-source software application for touch-screen smartphones that help children with autism and their caregivers to browse and combine images for communication faster than using PECS; 2) a reliable method for collecting data on the images used for communicating with the goal to track a child's progress; and 3) an online community that will help caregivers and practitioners work together to share knowledge and to improve outcomes for children with autism.

Methods: Because the final users of our smartphone application are the children with severe autism, we employed a participatory design using special education teachers as proxies to our target population. We worked with special education teachers in multiple public and private schools in North America to develop the smartphone application and the user community using a modular approach. This allowed us to incorporate new user feedback without having to re-develop the application each time.

Results: Pixtalk is open-source software application for smartphones with touch-screens. It is designed to allow users with autism and their caregivers to browse and combine images for communication. It can be used in therapy similarly to PECS but with access to an online library of images with the ability to efficiently add custom images for one or more students. PixTalk also provides the capability to log the images used and the sentences constructed by the children. Pixtalk is currently used by several children and their teachers in North America. An online community is ready to be launched. It allows the community of caregivers, health professionals, educators, and researchers to work in partnership on knowledge creation, ideas, problems and solutions.

Conclusions: Pixtalk and the online community are two technological solutions that provide an opportunity to improve the effectiveness of communication for children with autism, which will increase participation in a variety of communication settings with their families, friends and communities.

119.15 T15 Using Virtual Reality Enhanced Behavioral Skills Training to Teach Street Crossing Skills to Children and Adolescents with Autism Spectrum Disorders. T. R. Goldsmith*[1] and L. A. LeBlanc[2], (1)*Yale University*, (2)*Auburn University*

Background: Children with autism spectrum disorders (ASDs) often have poor safety skills due to insensitivity to subtle environmental cues and poor problem solving in the face of stressful tasks. Behavioral skills training (BST), consisting of instructions, modeling, rehearsal, and feedback, is effective for teaching safety skills and the effects improve with *in situ* training. However, creating realistic and safe contexts for rehearsal of skills such as street crossing may prove logistically difficult, if not impossible. Virtual reality (VR) affords a potential solution by allowing a child to interact meaningfully in an environment that is specifically designed to promote learning and generalization.

Objectives: To evaluate a partially immersive VR enhanced BST intervention for teaching safe street crossing to children and adolescents with ASDs.

Methods: A nonconcurrent multiple baseline design across 5 participants was employed to demonstrate experimental control in the virtual environment. Additionally, a within subject repeated measures design was used to determine the effects of training on skills in the natural environment. Data analysis was conducted via visual inspection of graphed performance.

Results: All participants mastered the skill set within the virtual environment and improved from pre-test to post-test in the natural environment, with some participants demonstrating treatment gains following the initial phases of BST.

Conclusions: VR affords incomparable control for arrangement of environments that best promote learning and generalization (e.g., removal and gradual introduction of distracting stimuli, exaggeration and normalization of critical stimulus features, and creation of limitless training examples to promote generalization). Results from the current study indicate that blending traditional teaching, in the form of BST, and technology, in the form of VR, is beneficial for children and adolescents with ASDs.

119.16 T16 Collectia Pilot: Supporting Data Collection in Special Education. A. Bozzorg*, V. Kantroo, A. Mansour, S. Pittman and G. D. Abowd, *Georgia Institute of Technology*

Background: Special education instructors need to collect academic and behavioral data to monitor the progress of their students, but require different evaluation methods than those used on the majority of students in public schools. However, the systems and tools currently in place to facilitate this activity are labor intensive and time-consuming, making the process of data collection burdensome. If data collection were made more efficient, there would be more time for teachers to devote to teaching and preparing lessons. The intent of our project is to alleviate the strain teachers have during the traditional data collection process and in turn, enable teachers to provide higher-quality learning environments.

Objectives: The project explores one way to give public school educators relief from the duties of data management and more time to focus on teaching. Another goal was to have teachers integrate the results of their data collection to tailor their teaching to better meet the needs of each student. Our team defined the different tasks that are performed by students, and created a workflow that extends current technology to assist teachers in their day-to-day work.

Methods: Potential users were recruited and interviewed during three phases of our design—1) to identify their needs, 2) after the conceptual designs were formulated, and 3) for prototype evaluation. Six special education professionals were recruited as participants in our focus group and survey. We gathered both subjective qualitative and quantitative information from these six. Our prototyped design was developed for the Tmobile G-1 Phone, using the Android platform.

Results: This formative study helped lay the groundwork for further development. We discovered the most important features of our design are the ability to communicate daily with parents, and to possess all students' information on one device (currently they have separate clipboards for each). While the educators were impressed with the directness of the touch interaction, they were frustrated with the intricacies of activating the touch (the device was not responsive to every touch). Our results showed that the users are interested in seeing the system developed to explore its potential. All of our participants expressed interest in the project and indicated that they would recommend this design to colleagues.

Conclusions: It was important for our design team to create a system that would be convenient to users. Since many teachers we interviewed expressed a great deal of annoyance with their current systems and indicated they procrastinate with data entry. It is our observation that the perceived convenience is of importance in motivating our users to become more active in the data collection process. By focusing on developing a system that maximizes perceived convenience, teachers could directly benefit from reduced stress while students could benefit through closer monitoring. We are interested in further investigating how to provide tools to educators to help maximize teaching time and effectiveness.

119.17 T17 An Extensible, Experimental Video Game for Autism Research and Therapy. M. K. Belmonte*, *Cornell University*

Background: Video games offer a way to combine the experimental control of precisely known stimulus timing and parameters with the ecological validity of engaging and motivating tasks. Recently we introduced a video game for autism research encapsulating measures of motion coherence threshold, distribution and shifting of visual spatial attention, auditory-visual integration, visual perceptual disembedding, motor inhibition, central coherence, and first- and second-order "theory of mind."
Objectives: Validate the game software via play-testing with children with and without autism spectrum conditions. Apply the game software with autism-spectrum probands, their clinically unaffected sibs, and unrelated normal controls, to test (1) whether the multiple levels of perceptual and cognitive performance measured by the game are correlated, (2) whether the same matrix of correlations identified in the autism-spectrum group exists in sibs and in controls, and (3) whether game-based training within each measure affects performance in correlated measures.
Methods: The game allows a broad range of cognitive and perceptual domains to be evaluated in a repeatable, learnable, anxiety-minimising context. Choices and decisions in the game are player-centred rather than computer-centred, and largely event-driven rather than time-driven. The game is extensible and inclusive; much of its artistic content has been provided by people with autism spectrum conditions as part of Google Project Spectrum, a project that teaches autism-spectrum schoolchildren how to use three-dimensional modelling software.
Results: The game will be demonstrated. Preliminary findings indicate correlations between low-latency (facilitated) responses for perceptual disembedding, narrow distribution and high shift latency of visual spatial attention, elevated (impaired) motion coherence threshold, and high-latency (impaired) "theory of mind" responses, in all groups studied.
Conclusions: The video game paradigm demonstrates correlations amongst autistic cognitive strengths and weaknesses extending not only within the autism spectrum but also in the broader autism phenotype and in normal cognitive variation. Video games hold strong potential for cognitive skills training not only for people with autism spectrum conditions but for all who can benefit from training. Future work will explore not only behavioural but physiological parameters within the game format.

119.18 T18 Baby Steps: Evaluation of a Computing System to Support Parent Reporting of Early Childhood Development. J. A. Kientz[1], R. I. Arriaga*[2] and G. D. Abowd[2], (1)*University of Washington*, (2)*Georgia Institute of Technology*

Background: Parents of children that are diagnosed with autistic spectrum disorders and other developmental disabilities often report that they saw early warning signs in their children with respect to cognitive and social skills. If these signs can be noticed and shared sooner, a diagnosis can be made earlier, which has the benefits of early intervention and access to services. Thus, accurate and timely record-keeping and review of children's developmental progress is an important goal. In addition, parents report that they are motivated to keep track of their child's development, but that they fail to do so because of forgetfulness or time constraints.

Objectives: We hypothesized that a computing system, called Baby Steps, could enable parents to track more of their child's developmental milestones more often and with higher confidence, and that this in turn could benefit parent-pediatrician communication.

Methods: We developed Baby Steps as a software application that stores developmental information about a child using the metaphor of a baby book. We studied the use of this system through a 3 month study of 8 families who were randomly assigned to use either an experimental or control version of the system. The experimental version included 4 additional features 1) a proactive reminder system, 2) the ability to create sentimental keepsakes, 3) online data sharing capabilities, and 4) an integrated device to capture videos and pictures. Interviews, software logs, and pre- and post-study questionnaires were used to measure records kept, timeliness, confidence, and communication with pediatricians.

Results: Compared to the control group, the experimental group accessed their child's records more frequently (C:9.75 days; E:17.5 days; $p<.05$) and recorded a higher number of records (C:48.5 milestones; E:90.5 milestones; $p = .16$). From pre- to post-study, pediatricians rated parents in the experimental group higher with regard to knowledge about their child's

development and the productiveness of their visit (C: +0.18; E: +0.51; p=0.01). Self-reported confidence in records-kept (on a scale from 1 to 5) increased from pre- to post-study for both groups (C: +0.53; E: +0.55).

Conclusions: As hypothesized, this study found that a well-designed computing system can improve aspects of parents' record-keeping. It is encouraging that parents in the experimental condition spent more time reflecting on their child's developmental milestones, which could perhaps lead to earlier communications of concerns to the pediatrician. Parents in the experimental condition were viewed as more competent by the physician, thus, this could perhaps lead to earlier coordination of intervention efforts for a child that is showing atypical development. Because of limited statistical differences between experimental and control group, future studies should further investigate this difference and whether this translates to sooner referrals to specialists. We also will explore how a computational system can be implemented and deployed to a larger population that may have limited access to technology in the home.

119.19 T19 User-Centered Design of Technology for Just-in-Time, in-Situ Exploration of Facial Affect for Persons on the Autism Spectrum. M. Eckhardt*, M. Madsen, Y. Kashef, A. R. Nasser, M. E. Hoque, R. E. Kaliouby, M. S. Goodwin and R. W. Picard, *Massachusetts Institute of Technology*

Background: Many people on the autism spectrum understand the semantics involved in social interaction; however, embodied information such as facial expressions, gestures, and voice often prove elusive. First-hand accounts from people with autism highlight the challenges inherent in processing these complex and unpredictable social cues. These challenges can be debilitating, complicating social interaction and making integration with society difficult. While many intervention methods have been developed to provide help, the majority fail to include rich, real-world social interactions in their methodology.

Objectives: Our goal is to develop a technology-based intervention that helps individuals on the autism spectrum capture, analyze, systemize, and reflect on social-emotional signals communicated by facial and head movements in natural, everyday social interactions. Our approach utilizes an ultra-mobile computer customized with a video camera and pattern analysis algorithms that can automatically identify facial expressions using facial feature tracking. In an effort to make our system robust to real-world conditions and usable by individuals with cognitive, motor, and sensory impairments, we have engaged in a number of user-centered design sessions with people on the autism spectrum and their caregivers.

Methods: We conducted five usability sessions with seven verbal adolescents on the autism spectrum and their teachers to address various hardware and software functionality issues related to our system.

Results: Our initial interface design using facial expression graphs and points superimposed on the video to indicate features on the face was confusing and not engaging enough for the participants. Based on iterative feedback, interactive affective tagging components were added and the interface was made customizable to suit each participant's interests and difficulties in recognizing particular facial expressions. For example, some participants were good at recognizing happiness, sadness, and anger. For those participants, we were able to instantly customize the interface to handle a more challenging set of affect labels, such as confusion and excitement. In terms of form factor, many participants found the mobile computer's keyboard and track pad distracting. To overcome this, we made custom covers that shield exterior input controls and utilized the ultra-mobile computer's touch screen to input data. We also adjusted the placement and size of touch screen buttons to allow participants to use their thumbs for interaction. Finally, some participants had difficulty reading the text labels describing identified facial expressions. We are currently exploring the use of images instead of text to accommodate reading difficulties.

Conclusions: The user-centered design sessions provided insights into the usability of the system and were critical to the development of our technology, underscoring the importance of including people on the autism spectrum and their caregivers in the design process of new technologies. For these technologies to be effective, they need to accommodate the perceptual, motor, and cognitive disabilities of their users. An experimental evaluation of our

redesigned system is forthcoming to determine if just-in-time, in-situ assistance can help facilitate learning of facial expressions and underlying emotions for persons on the autism spectrum.

119.20 T20 An Initial Investigation Using Augmented Toys and Statistical Models to Automatically Categorize Object Play Behaviors. T. L. Westeyn, T. E. Starner, G. D. Abowd*, R. I. Arriaga and P. W. Presti, *Georgia Institute of Technology*

Background: The way in which infants play with objects can be indicative of their developmental progress and may serve as an early indicator for autism spectrum disorders. To better quantify these indicators, retrospective video studies have been used to correlate differences in object play among infants with subsequent diagnoses. Such studies require laborious video annotation. While computers can assist in the coding process, it remains a bottleneck where researchers must repeatedly inspect video at speeds much slower than real-time to indicate points of interest. To help alleviate this bottleneck we are exploring automated methods for collecting and annotating developmental data during object play. In particular, we are using computer algorithms that leverage statistical models to process data collected from our toys containing embedded wireless sensors.

Objectives: Our goal is to use neurotypical adults to determine if wireless sensors embedded in toys can provide sufficient data for the creation of statistical models of play behaviors. We will also automatically provide quantitative measures of object play similar to those produced by coding schemes used in retrospective video studies.

Methods: Five neurotypical adults were recruited. Each subject participated in a minimum of two play sessions lasting 7 – 26 minutes (μ=16.32 minutes, σ=7.17 minutes). Five augmented toys collected data at each session as participants performed loosely defined scenarios that included exploratory, relational, and functional play tasks. A total of 12 sessions were completed resulting in 3.8 hours (228.49 minutes) of sensor data containing 3,999 instances of object play. The data was independently labeled by two people with 24 possible primary actions for each toy (120 distinct classes). Statistical models were constructed using aggregate features computed over short temporal windows. Models were trained for specific play behaviors, toys, and a general binary categorization of relational play, using the iterative AdaBoost framework.

Results: Models trained to identify the 24 different instances of object play (across all participants) for 5 distinct toys performed with an average frame-level accuracy of 41.7%, while models trained to identify the 24 play behaviors regardless of the toy's form factor performed with an average accuracy of 30.1%. These numbers improve by approximately 10% if the models are trained in a user-dependent fashion. The more generalized binary model had an average recall of 99.0% for instances of relational play (only missing 1.0%). However, a high number of false detections were also identified, causing very low precision.

Conclusions: While more research is required, early results demonstrate that augmented toys can capture sufficient information about object play allowing the generation of statistical models which automatically filter data for later review. Our models seldom omit play events, however extra events are detected. Researchers may easily dismiss these false detections as erroneous. Our results indicate that automatic processing methods have the potential to dramatically reduce the amount of time researchers spend coding data and allow them to more rapidly ask and answer relevant questions about object play and how it relates to a diagnosis of autism spectrum disorders.

119.21 T21 Cognitively Accessible Self-Management: Picture Planner Icon-Based Personal Organizer. T. Keating*, *Eugene Research Institute*

Background: Our development work focuses on cognitively accessible self-management software for users with significant cognitive disabilities, many of whom remain excluded from the benefits of information technology because commercial software is not accessible due to its complexity and dependence on the user's reading ability. There is also a lack of cognitively accessible software targeting functional user needs such as activities of daily living (Burgstahler, 2003; Wehmeyer, 1999).

Objectives: Eugene Research Institute together with Cognitopia Software has recently produced a cognitively accessible personal activity organizer called Picture Planner (Keating, 2006), an icon-driven application whose objective is to enable users with autism and other cognitive disabilities to create activity schedules. It incorporates several design features to facilitate use by individuals with little or no reading ability and

those for whom typical user interfaces are too complex: the use of multi-modal icons providing image, text, and text-to-speech information; single-click operability; and metacognitive support for the information management challenges experienced by many users with cognitive disabilities.
Methods: Picture Planner's metacognitive interface design anticipates information management challenges experienced by individuals with autism. A typical user of a paper or electronic organizer might enter a word or two in a time slot, relying on that prompt to cue a set of related implications that is retained in memory and retrieved as needed to accomplish an activity. For our target users, competently constructing activities must be more explicit: processing not just "what" activity is scheduled, but making explicit the many elements of an activity that bear on its successful completion: What activities are available to choose from? How much money do I need? Who am I doing it with? When and where does it happen? How will I get there? What things should I bring? What clothes are appropriate? Many individuals benefit from having these choices explicitly prompted, with intelligently presented and accessible ways to choose among options in each domain. In this application, the user is systematically presented with and "stepped through" each of these considerations.
Results: A non-experimental post-test only evaluation was conducted in which users were taught how to use the software over a period of 8 weeks. They were then given a detailed activity to schedule and scored on whether they completed each step of the sequence and what kind of verbal or physical assistance was needed. The participants included transition students and young adults with autism, intellectual disabilities, and traumatic brain injury. A key finding was that with only limited instruction typical of a weekly classroom format (one half hour per week over 8 weeks) individuals with significant cognitive disabilities including autism averaged 54% successfully completed steps of a complicated activity planning task, with either no assistance or only nonspecific verbal prompts about activity details (N=28; Range=29-82%).
Conclusions: Individuals with autism and other cognitive disabilities can learn to use cognitively accessible self-management software. As important, the software served an important function in structuring the interaction between assistant and user in a way that enhanced self-determination, communication, and self-esteem.

119.22 T22 Using Computer Software to Address Emotion Recognition and Social Skills. P. G. LaCava*, *University of Kansas*

Background: Recognizing others' emotions and mental states is key to social interaction. This ability to "mind read" has been found to be impaired in many individuals with ASD (Baron-Cohen, 1995, 2003). Various computer programs have been used to teach emotion/social skills (Moore et al., 2005; Silver & Oakes, 2001). One such program, Mind Reading: The Interactive Guide to Emotions (Baron-Cohen et al., 2004), has been used with adults (Golan & Baron-Cohen, 2006) and children with ASD (LaCava et al., 2007) to improve face and voice emotion recognition. Objectives: The purpose of this research was to investigate the use of the Mind Reading software to improve social/emotional skills for students with ASD in school settings. Methods: Study 1 was a multiple baseline across 3 participants (mean age=10.66) design used to investigate if Mind Reading use would improve emotion recognition skills and social behavior. Computerized emotion recognition testing was also conducted pre and post intervention. The two girls and one boy independently used Mind Reading in a school setting for 10 weeks (M=8.78 hours). Observations (using interval recording) of social interaction were made during baseline and intervention phases in the school setting. Study 2 was a replication of Study 1. The same design and procedures were followed except that the four male students (mean age=8.5 years) used Mind Reading with an adult tutor for 7 to 10 weeks (M=12.5 hours). Results: Each participant in both studies improved on at least two emotion recognition tests as well as increased positive social interaction and/or decreased negative social interaction in natural settings. Emotion recognition improvements in Study 2 were greater than Study 1. Anecdotal reports from parents, students, and school personnel support the use of Mind Reading in helping individuals to increase social interactions, use emotion vocabulary and improve emotion recognition. Conclusions: Use of the software was associated with gains in emotion recognition skills. Mind Reading use with an adult tutor brought about the greatest changes from pre to post testing. Observations of social behavior in natural settings revealed increases in positive or decreases in negative social interaction but the evidence was not strong enough to claim a causal

relationship between use of the software and observed behavior change. Future research is merited to continue exploring the use of this and other technology with co-occurring interventions as a means to improve emotion recognition and social behavior.

119.23 T23 Automated Acoustic Analysis of Affective and Pragmatic Prosody in ASD. E. T. Prud'hommeaux*, J. P. H. van Santen and L. M. Black, *Oregon Health & Science University*

Background: Autism Spectrum Disorders are associated with deficits in affective and pragmatic prosody. An examiner's evaluation of prosody for a particular affect or social situation in real time is subject to influence from external factors. The examiner is aware of the subject's current mood and has likely noted how the subject spontaneously expressed affect previously. A clinically trained examiner might also entertain a hypothesis about the subject's diagnosis. Such biases could be moderated by including scores from an automated analysis of acoustic features that yields results similar to those produced in a "blind" assessment.

Objectives: The goals of this study are 1) to ascertain the reliability of real-time judgments of prosody expressing affect and pragmatic style; 2) to determine whether our complex automated measures of acoustic features can accurately identify different affects and styles; and 3) to explore the ability of these scores to distinguish TD subjects from subjects with ASD.

Methods: Responses for these two tasks testing affective and pragmatic prosody were scored by clinicians during examination, by six naïve listeners in a web-based, "blind", perceptual experiment, and with automated objective measures of acoustic features:

(i) Pragmatic Style (use appropriate prosody talking to an adult or baby; adapted from Paul et al. 2005)
(ii) Affect (repeat a phrase with one of four affects)

During examination, clinicians immediately assessed the correctness of each response, yielding real-time scores.

In the perceptual experiment for Pragmatic Style, six judges listened to recordings of minimal pairs of responses and selected the infant-directed utterance. In the Affect experiment, judges listened to an utterance and selected the perceived affect from a list of four (angry, sad, scared, and happy), along with their confidence in their selection.

In the automated analysis, quantitative features based on pitch, energy, and spectral balance were computed from recordings of the children's responses and combined using multiple linear regression to create a single complex score for each utterance.

Results: A per-utterance and per-speaker analysis of both tasks revealed that the objective digital measures generally correlated with the consensus scores as well as the judges correlated with one another and with the consensus scores. The correlations of the object measures were also consistently better than the correlations of the real-time scores with the judges' scores.

In the Pragmatic Style task, both the consensus scores and the objective scores showed TD subjects significantly outperforming ASD subjects. These results in the real-time scores were not significant.

In the Affect task, consensus scores distinguished the TD group from the ASD group only for happiness and sadness. Both the objective and the real-time scores distinguished TD from ASD for happiness but not for sadness. Real-time scores found between-group differences in anger, which was not confirmed by the consensus scores, possibly illustrating bias in real-time scores.

Conclusions: The objective acoustic measures of affect and pragmatic style expression were comparable in reliability to "blind" consensus subjective scores and superior to real-time clinical judgments in terms of both accuracy and ability to distinguish between the two diagnostic groups.

119.24 T24 Automated Identification of Stress and Focus Assignment. E. T. Prud'hommeaux*, J. P. H. van Santen and L. M. Black, *Oregon Health & Science University*

Background: Evaluation of expressive prosodic ability plays an important role in the diagnosis of neurodevelopmental disorders such as ASD. Existing methods for assessing prosodic performance require that judgments be made at the time of examination. Such real-time subjective judgments are typically not verified, since verification by one or more additional listeners is time-consuming and costly. Accurate automated analysis of prosody could increase both

efficiency and accuracy in clinical evaluations of prosodic ability.

Objectives: The goals of this study are 1) to determine the reliability of real-time judgments of stress and focus assignment, and 2) to determine whether our complex automated measures of the acoustic features associated with stress and focus are comparable to consensus listener judgments and real-time clinical assessments.

Methods: Responses for the following three tasks were scored by clinicians during examination, by six naïve listeners in a web-based perceptual experiment, and with automated objective methods:

(i) Lexical Stress (repeat a disyllabic nonsense word with initial or final stress)
(ii) Emphatic Stress (repeat a four-word sentence with emphasis on one word; adapted from Shriberg et al. 2001, 2006)
(iii) Focus (correct an inaccurate description of a picture by emphasizing the correct word; adapted from PEPS-C (Peppé & McCann 2003))

During examination, clinicians immediately assessed each response for each stimulus as either correct or incorrect, thereby producing real-time scores.

In the perceptual experiment, six judges listened to recordings of "minimal pairs" of responses for each of the three tasks, with each pair from a single speaker with the same content but different target prosody. The judges were asked to identify the intended meaning of the two utterances (e.g., of two recordings, which one was meant to be "BLUE cow" rather than "blue COW").

For the automated analysis, pitch and energy trajectories and phoneme duration information were extracted from recordings of the children's responses and analyzed using an innovative "dynamic difference" measure that captures the difference in the pitch and amplitude dynamics of the two recordings in a minimal pair. Measures of melody, timing, and intensity were combined using multiple linear regression to create a single complex score for each utterance.

Results: For all three tasks, the combined objective measures correlated with the consensus scores at least as well as the judges correlated with one another and with the consensus scores. These correlations were also substantially better than the correlations between real-time scores and the consensus scores. A per-speaker analysis revealed similar results: objective measures correlated with consensus scores as well as the individual judges and substantially better than the real-time scores.

Conclusions: The automated digital measures of stress and focus assignment were shown to be comparable in reliability to consensus subjective scores and superior to real-time clinical judgments on both a per-utterance and a per-speaker basis. Including automated objective measures of prosody alongside traditional real-time judgments could enhance both accuracy and reliability in clinical assessments of prosodic ability.

119.25 T25 Using a Behavioral Imaging Platform to Develop a Naturalistic Observational Diagnostic Assessment for Autism. C. J. Smith*[1], S. E. Ober-Reynolds[1], K. Treulich[1], R. McIntosh[1] and R. Melmed[2], (1)*Southwest Autism Research & Resource Center*, (2)*Southwest Autism Research Center and Melmed Cente*

Background: The Autism Diagnostic Interview-Revised (ADI-R) and the Autism Diagnostic Observation Scale (ADOS) have strong psychometric properties and are the current gold-standard assessment tools for autism. However, these instruments have several problematic features: 1) they both require training and extensive practice for a rater to develop proficiency; 2) the ADI-R relies on a combination of a caregiver's interpretation of behavior, her ability to clearly articulate descriptions of behavior, and a rater's ability to probe effectively; 3) an interview can take between 1.5 to 3 hours to complete; 4) the ADOS provides 30 minutes to observe behavior and relies on structured probes; and 5) while the ADOS can classify a subject with autism or autism spectrum disorder (ASD) based on atypical behaviors related to socialization and communication, no repetitive behaviors are considered in the process. Excluding one required behavioral domain can lead to an incomplete clinical profile for the individual. An improved diagnostic measure would rely on observed behavioral examples that occur during routine natural settings and provide sufficient information to diagnose autism. This procedure would provide a more accurate clinical profile for the individual. Objectives: To design a reliable and valid diagnostic procedure for classifying individuals

with autism based on observation of typical and autism-related behaviors that occur in naturalistic settings and requires significantly less time than the ADI-R and ADOS.
Methods: Participants were five children with autism, age four and under, and their caregivers. ADI-R and ADOS assessments were previosuly completed. Parents were asked to: 1) record their child for 8 to 10 minutes in four settings: mealtime, play with peers, unstructured play, and problem time, on two separate days, with an inconspicuous Flip Video™ camera; 2) interact with their children as they would normally do in each setting; and 3) upload videos from their home to B.I. (Behavior Imaging) Care's platform for rater review. Three ADI-R and ADOS reliable raters reviewed each of the videos online from multiple locations. The raters used B.I. Care's video tagging and annotations tools to comment on typical behaviors as well as autism related behaviors. The tagged autism related behaviors were then used to support DSM IV criteria for autistic disorder.
Results: Each child assessed through this method met full DSM IV criteria for autistic disorder. Previously, five children met criteria for ADI-R autism, three met criteria for autism on the ADOS, and two met criteria for ASD.
Conclusions: This procedure relies on direct behavioral observation that occurs in the naturalistic setting, permits for behaviors to be observed over time, was completed in <60 minutes, and was concordant with ADI-R diagnosis. Additionally, this method provides an opportunity to quantify the amount and type of typical behavior that is exhibited by the child, which, combined with the measure of autistic behavior may translate into a measure of severity for the disorder in each child. Work on this project is continuing as we collect a larger sample of subjects and we plan to measure the reliability of raters who are untrained on the ADI-R and ADOS.

119.26 T26 Toward Designing Interactive Technologies for Supporting Research in Autism Spectrum Disorders. D. Feil-Seifer*, M. P. Black, M. J. Mataric and S. Narayanan, *University of Southern California*

Background:

Mounting evidence suggests that children with autism spectrum disorders (ASD) tend to increase their levels of social behavior when interacting with a robot. There are many explanations for the possible effects that a robot has on children with ASD. Many individuals with ASD have shown the ability to display higher-level behaviors in structured social settings. Since children with ASD have difficulty with the self-initiation of social behavior, and that initiation of behavior is important for social skill development, a robot that helps with initiation of social behavior could be potentially valuable in both research and intervention.

Objectives:

The aim of this work is to better define the link between interactive robots and increased social activity in children with ASD. Specifically, we wish to determine if a link exists, and if so, what elements of a robot's form and function (contingency, anthropomorphism, embodiment, etc.) correlate with changes in social behavior. We also aim to detect and interpret the child's interactions, especially social behavior relevant to ASD (body position, head direction, gestures, vocal prosody, etc.). Finally, we are designing a robot system that can act appropriately in a social setting that could be used to augment established diagnostic and therapeutic regimens for children with ASD.

Methods: To accomplish these objectives, we are designing an interactive robot-based experimental environment. The robot consists of a mobile base and a human upper-torso with actuated arms, neck and face. The robot can use movement and has speakers to play synthetic and pre-recorded speech sounds. The robot can also be equipped with relevant toys, such as a bubble-blower. We have created variations on this design to isolate contingent from random behavior, anthropomorphic from more mechanical appearance, and embodiment from non-embodiment (e.g., a virtual agent on a screen). The robot and the environment are both instrumented with cameras and microphones to capture the interactions from multiple perspectives.

We are planning on single and multi-session within-subject experiments to test the effectiveness of the various robot configurations. We wish to observe changes in both human-human and human-robot interaction, so a parent will always be in the room; in some cases, a clinical psychologist may also be present. We will evaluate the interactions using established

human-rated behavior metrics. We are also developing means for autonomously detecting and quantifying social behavior of children from the multi-modal audio-video signals. This automatic sensing and interpretation could be used to measure interaction quality on-line, and could be a valuable tool for psychologists/therapists in the future.

Results:

Our experiments are currently in progress, so we will report results in the future.

Conclusions:

At the workshop, we plan to share our experiences with the iterative design of these systems and the insights and findings from our ongoing experiments with children with ASD.

119.27 T27 Interactive and Collaborative Classroom Visual Schedules. M. Yeganyan*, S. H. Hirano, D. H. Nguyen and G. R. Hayes, *University of California, Irvine*

Background:
Visual schedules have been in use as a best practice in schools for many years. These artifacts use words and images to represent activities that will take place (or have taken place) arranged in temporal order to augment understanding of time, events, and places. Research has shown that the use of visual schedules can improve communication with children with autism spectrum disorder (ASD). Often, however, these visual schedules are not interactive and interesting enough to draw and maintain attention; they can be out of date or inaccurate; and they do not support communication and collaboration surrounding activities. Handling these challenges necessitates an immense amount of manual effort by teachers and aides. To offset this burden, we have created innovative computing technologies that we are using to simplify schedule creation and generate useful data that teachers and other caregivers can analyze.

Objectives:

Design and implement a visual scheduling system for classrooms to support children with autism and expand or refine current teaching techniques to make use of this new system. Demonstrate these schedules in use sessions by teachers.

Methods:

We used paper and simple digital prototypes during sessions in autism classrooms and interviews with teachers and autism specialists. During the sessions, we iteratively developed a system that not only mimics the analog visual schedules currently in use but also provides new features. For example, the system provides students with personal devices that interact collectively with a large shared screen at the front of the room. We are collecting information about system usage and practices of teachers and students during demonstration visits and initial use in classrooms. In particular, we are interested in understanding the potential for social learning as students, teachers, and aides are able to see responses from students who may be struggling on particular activities as well as those who have mastered them.

Results:
By spending time in the field with teachers, specialists, and children with autism, we have been able to understand and compile information about the design of interactive visual schedules. These electronic visual schedules can assist teachers in managing their classrooms, in not only setting up exercises but also running them and keeping records that would otherwise be unfeasible. Finally, using both shared large displays for the whole class and smaller networked systems for individual children, we enable new interactions in classrooms, including social and peer learning as well as more efficient and rapid feedback for students and staff about individual progress and abilities.

Conclusions:
We have designed and developed an interactive visual scheduling system based on extensive in-school interviews and observations. This system replaces and enhances the features of analog visual schedules in digital form. Through this new system, we also enable new ways of keeping records by automatically logging all interactions with the system and new forms of teaching and learning by dynamically sending and receiving visual information to the students' networked personal devices.

119.28 T28 Rich Spontaneous, Social Engagement with a Dinosaur Robot. E. S. Kim*[1], D. Leyzberg[1], E. Short[1], R. Paul[2] and B. Scassellati[1], (1)*Yale University*, (2)*Yale University School of Medicine*

Background: Children with ASD exhibit atypical social behaviors, including reduced eye contact. They also have been shown to take special interest in mechanical objects, including robots.

Objectives: We compare the social behaviors observed in children with ASD during interaction with a socially expressive Pleo robot, to those seen in interaction with an adult. Our long-term goal is to assess the feasibility of robots as therapeutic tools that promote conventional social behavior.

Methods: We compared social engagement in verbal interactions between four males with ASD, and a socially expressive robot, against that in structured interviews with a trained experimenter, in the Yale In-vivo Pragmatics Probe (YIPP). Participants included one nine year-old, ten year-old twins, and a 15 year-old.

The Pleo robot is a 2-foot, commercially distributed, toy dinosaur robot. Custom software, behavior, and sounds afford Pleo social expressiveness. The robot's behavior is triggered by an experimenter with a hidden remote control. The robot's responses and vocalizations are designed to engage and sustain social interactions with the child.

Pleo walked across a 4'-long mat illustrated with a jungle scene. For each participant, Pleo crossed four painted rivers. At each, Pleo stopped walking and exclaimed in surprise. Participants were instructed to help Pleo walk across the mat, by talking in an encouraging tone of voice when Pleo expressed fear of water. If the participant did not respond encouragingly, he received an increasingly restrictive sequence of cues suggesting he help Pleo, including instruction and finally modeling from the experimenter.

In YIPP, participants spoke freely on any subject. They were confronted with (1) a tacit opportunity to help the experimenter solve problems and (2) role-playing scenarios expecting choice of pragmatically appropriate language and affective expression.

Pleo and YIPP interactions were video-recorded. An independent experimenter, who was blind to diagnosis, annotated social behaviors in the videos. Eight 30-second clips were sampled throughout each video to normalize for differing interaction durations. For each 30s clip, eye contact and affective prosody were annotated.

Results: Pleo interactions lasted 5-13 minutes. YIPP interactions lasted 16-20 minutes.

For all participants, we observed longer eye contact with Pleo (m = 19.9s, sd = 8.2s) than with the human YIPP interviewer (m=2.0s, sd = 1.4s), for the maximum-duration, sustained eye contact episode in each 30s clip.

For one twin, the annotator described greater variety in the types of affect expressed in prosody (eg, chiding, frustrated, soothing), in his speech to Pleo than to the YIPP interviewer (17 versus 10 total, over all clips). For the other twin, the average intensity of his affective prosody, rated on a scale of 0 (no affect) to 2 (strongly emotional), was greater in speech to Pleo (m=1.8) than in speech to the YIPP interviewer (m=1.2).

Conclusions: All four ASD participants spontaneously exhibited longer eye contact with the Pleo robot than with a human. We have also observed greater variety and affective intensity in prosody, during interaction with Pleo, for some participants.

119.29 T29 Inferences on Cognition in Nonverbal Children Via Real-Time Analysis of Eye Gaze. J. Munson*, *University of Washington*

Background:

The assessment of cognition and language in children with autism who have little spontaneous communication presents clinicians, educators, and researchers with numerous challenges due to the nature of impairments in autism and characteristics of the assessment situation itself. Most standardized assessments involve an examiner, whom the child does not know, who attempts to elicit responses from the child while referencing various test materials. For this common methodology to yield meaningful results it requires a foundation of an extended bout of successful responsive joint attention by the child. Without this foundation these tests are simply unable to provide much meaningful information often resulting in the commonly observed "floor score."

Objectives:

As an example, recent research at the University of Washington Autism Center, 483 cognitive assessments of preschoolers with autism spectrum disorders have been conducted using the Mullen Early Scales of Learning. Thirty percent of these children obtained a composite score at the floor of the scale while 63% had at least one subscale at the floor. Given the design requirements of many research protocols, children who fail to obtain some minimum threshold are often excluded from participation. Thus, we have a limited number of tools that provide insight into why these children struggle with these tasks. In addition, traditional examiner-driven assessments provide little information regarding the type of information-processing tasks these children spontaneously solve when interacting with their environment. As a field we need to capitalize on the innovative use of technology to provide child-driven experiences that aid our understanding of the cognition of this understudied group of children.

Methods:

This project uses eye-tracking and real-time 3D graphics to provide a virtual environment the child can visually explore at their own initiative. The child watches virtual scene presented via a 3D graphics engine used in contemporary video games while a remote infrared camera eye tracker (SmartEye Pro 5.3) estimates where the child is looking. Various scenarios will be presented to the child including an onscreen character speaking and presenting written language, as well as physics-based interaction of objects (e.g., stacked blocks falling, ball rolling). The child's gaze location is fed back to the display computer (@60Hz) in real-time allowing aspects of the virtual scene to be contingent on the child's gaze behavior. No explicit behavioral response from the child is required beyond sitting in the chair and watching the scene.

Results:

The demonstration of this system will include two computers, one running the SmartEye software from a recording of a child with autism with very limited expressive communication who is watching the virtual scene. The second computer will run the display program and will receive input from the SmartEye computer. This will completely simulate the system in operation. Summaries of gaze behavior during different phases of the scene will be provided.

Conclusions:

It is hoped this demonstration can provide the field one example of an assessment methodology that can allow the exploration of cognition in children with autism who historically have been an understudied but very important group.

120 Poster III

120.01 1 Parent and Child Factors Associated with Sleep Problems in Pervasive Developmental Disorders, Down Syndrome and Intellectual Disability. A. Richdale*[1] and A. Robinson[2], (1)*La Trobe University*, (2)*Austin Health*

Background:

Parent-reported sleep problems are common in children with a developmental disability, particularly those with a pervasive developmental disorder (PDD). Child sleep difficulties have been associated with challenging behaviour, child psychopathology and parent stress, but whether or not the relationship of these factors with child sleep differs across developmental disorders is largely unexplored.

Objectives:

The aim was to examine whether parent or child factors purported to be associated with problematic child sleep differed for children with PDD, Down syndrome (DS) or intellectual disability (ID).

Methods:

This was part of a larger study examining the influence of parent and child characteristics on sleep in children with a developmental disability. Parents (N = 76) completed demographics, Behavioral Evaluation of Disorders of Sleep (BEDS), Developmental Behavioural Checklist (DBC), Adaptive Behavior Assessment System, Eysenck Personality Questionnaire-R, Parenting Sense of Competence, Parenting Hassles Scale, Levenson's Locus of Control Scale, and rated perceived control over their child's sleep and behaviour. Using BEDS scores children (M = 10.6 years, SD = 4.4) were classified into 3 groups: Recognised Sleep Problem (RSP), Unrecognised Sleep Problem (USP), and No Sleep Problem (NSP). Within the 76 families, three main developmental groups (N = 62) were also

identified PDD (n = 30), ID (n = 18) or DS (n = 14). A series of Kruskal-Wallis tests and multiple comparisons using Mann-Whitney tests (Bonferroni adjusted alpha = .017) were used to examine differences between the 3 sleep groups within each developmental group for these parent and child measures.

Results:

For the PDD group the sleep groups differed significantly on the DBC total score, the DBC self-absorbed, depression and hyperactivity subscales and the DBC autism screen. Hyperactivity differed for the RSP and USP, and RSP and NSP groups whereas for the other DBC scores only the RSP and NSP groups differed. For the DS group the sleep groups differed on parents' perceived control over their child's sleep behaviour with the RSP and NSP groups differing. No other child measures and no parent measures differed for the PDD or DS groups. No significant sleep group differences were found for any measure for the ID group.

Conclusions:

Factors associated with sleep problems differed for children with a PDD, DS or ID. Sleep problems were related to behaviour for children with a PDD, particularly hyperactivity, but this was not so for DS or ID. Thus behavioural issues play a significant part in sleep difficulties in children with a PDD compared with other disabilities. This underscores that examining sleep and behaviour in mixed disability groups may obscure findings. It reinforces that when examining relationships between child sleep and parent or child behaviour, developmental disorders should be investigated separately. Further research with larger sample sizes is needed to confirm our results.

Author Note: Both authors were formerly at RMIT University. These data are from Dr. Robinson's dissertation, conducted there with Dr.Richdale as senior supervisor.

120.03 3 Study of Parental Perception of Symptoms and Satisfaction with Disclosure of the Diagnosis of An Autism Spectrum Disorder. T. Miyachi*[1], M. Kamiya[1], Y. Yoshihashi[1] and M. Tsujii[2], (1)*Osaka-Hamamatsu Joint Center for Child Mental Development*, (2)*Chukyo university*

- **Background:** The early diagnosis and the familial acceptance of child's developmental disorder are very important for the support of children with autism spectrum disorder (ASD). We need to know about the first parental perception of relevant symptoms in children with ASD and the effect of early diagnosis on the parental acceptance.

- **Objectives:** This present study determined 1) when did the parents first noticed developmental problems with their child; 2) what kind of symptom the parents noticed; 3) when the parents were first notified of the child having a diagnosis of ASD; 4) whether the families satisfied with disclosure of the diagnosis of an ASD.

- **Methods:** We enrolled 120 parents who are members of a non-profit organization for families having a child with ASD (104 boys, 16 girls). They were willing to fill out a self-report questionnaire on the disclosure of the diagnosis and their acceptance of it.

- **Results:** The average age of the children of participants at the study was 12.3 years. Most children were elementary school students, and of those, 67% attended normal classes and 23% attended special classes. Most parents responded that they first noticed problems with their child's development between the ages of 18 and 36 months, and a considerable number already noticed symptoms before 18 months. Indications appearing before 18 months included not aligning glances, not responding to hugs, late development of movement, being poor at action and activities, staring at walls, and playing in strange ways. Symptoms noticed between 18 and 36 months included late development of language and easily becoming lost, and above 36 months they included poor adaptation to group life and the inability to get along with children of the same age. Parents waited up to about 40 months after noticing symptoms before going for a diagnosis. Diagnoses of autism were significantly faster than other diagnoses (Asperger syndrome, atypical autism and ASD tendency). There was a tendency among those whose children were diagnosed at a young age to respond

that "diagnosis came at a good time and it was helpful in making decisions afterwards." Many parents wanted to know not only the name of the diagnosis but what the prospects were, what they should do concretely, and what sort of social resources are available to aid in raising their children. In addition, some dissatisfied voices also expressed worrying too much as they were given no concrete advice and told only to wait and see, although they sought expert advice.

- **Conclusions:** The results underscore the importance of an early diagnosis and interactive process between families and practitioners to help the parents satisfied with the diagnosis.

120.04 4 Use of Complementary and Alternative Medicine in Children with Autism: Associations with Ethnicity, Child Co-Morbid Symptoms and Parental Stress. M. D. Valicenti-McDermott, L. Bernstein, B. M. Burrows, K. Lawson, M. Schechtman, R. Seijo, L. H. Shulman* and S. Shinnar, *Albert Einstein College of Medicine*

Background: Families of children with an Autism Spectrum Disorder (ASD) frequently engage in the use of Complementary and Alternative Medicine(CAM). Little information is available about frequency and types of CAM used in an inner city, ethnically diverse population and associations with specific child co-morbid symptoms or parental stress.
Objectives: To examine the use of CAM therapy in a group of families of children with an ASD and to assess the relationship of CAM with feeding, gastrointestinal, sleeping and behavioral difficulties and parenting stress.
Methods: Cross sectional study with structured interview in 100 children with prior diagnosis of ASD. Interview includes: CAM questionnaire, Gastrointestinal (GI)Questionnaire, Childs Sleep Habits Questionnaire, Aberrant Behavior Checklist (ABC) and Parenting Stress Index(PSI). Statistical analysis included chi-square, t test, Pearson Correlation and Linear Regression.
Results: To date we have recruited 41 children, mean age 8 3 yr. Families self identified as 15% White, 44% Hispanic and 24% African-American. Use of CAM was reported in 66 % of the sample, including supplements (44%), sensory integration (37%) and gluten-casein free diet (29%). The number of different CAM therapies used ranged from 0 to 8. Compared to White mothers, Hispanic mothers used fewer types of CAM therapies (3.2 vs. 1.2 p=0.02); this association persisted after adjusting for level of maternal education. CAM use was associated with higher levels of parental concerns about ASD diagnosis (r=0.3 p=0.03), and with parental stress, as measured by PSI (r=0.3 p=0.04). If the child had at least one behavioral problem as measured by the ABC, family was more likely to use more types of CAM (1.2 vs. 0.2 p=0.01). No association was observed with time since diagnosis of ASD, food selectivity, GI symptoms or sleeping problems.
Conclusions: At least 66% of an inner city, ethnically diverse population of families of children with ASD engaged in CAM therapy. In our cohort, the use of CAM seems to be related to ethnicity (reduced frequency in Hispanic families), parental concerns about childs diagnosis, parental stress and child behavioral problems.

120.05 5 The Relation Between Family Resources, Child Severity, and Parenting Stress in Parents of Young Children with Autism. G. A. Levine*, J. H. Foss-Feig and W. Stone, *Vanderbilt University*

Background:

Parents of children with autism report higher stress levels and lower perceived parenting competency relative to parents of children with other developmental disabilities and children with typical development (Bromley et al., 2004; Rodrigue et al., 1990). One source of parenting stress is worry about the child's future independence (Koegel et al., 1992), which is partially contingent upon the child's receipt of and response to intervention. Although intensive early intervention has been associated with improved developmental outcomes for children with autism, the associated time commitment and financial burden can be major stressors for parents. Moreover, recent research has suggested that when parenting stress is high, interventions for children with autism, particularly those that are very time-intensive, are less effective (Osborne et al., 2007). Therefore, clarifying the relations between family resources, autism severity, and parenting stress may provide important information for understanding potential barriers toward accessing and implementing optimal interventions for young children with autism.

Objectives:
To examine the extent to which autism severity and family resources are related to parenting stress.

Methods:

Family resources and parental stress were assessed in the families of 27 young children with autism (mean CA = 32.4 mo; range = 24-46 mo) using the Family Resource Scale (FRS) and Parenting Stress Index – Short Form (PSI-SF), respectively. Most or the respondents (93%) were mothers. Autism diagnoses were confirmed using the ADOS; the Childhood Autism Rating Scale (CARS) was also completed by a clinician to rate severity of autism symptomatology. Family resources on the FRS are separated into four categories: resources related to 1) time; 2) money; 3) basic needs; 4) the child. Bivariate correlations were conducted between family resources, parenting stress, and autism severity measures to determine the relations between these constructs.
Results: 37% of parents had clinically elevated PSI-SF scores. Results revealed a significant correlation between lower family resources and higher parenting stress ($r=-.626$; $p=.001$). Specifically, higher parenting stress was associated with fewer resources in the areas of time ($r=-.660$; $p<.001$) and money ($r=-.581$; $p=.006$), though not with resources related to basic needs or child-related factors. The relation between autism symptom severity on the CARS and higher parenting stress approached significance ($r=.367$; $p=.071$). In addition, increased autism severity was associated with lower overall resources ($r=-.542$; $p=.003$).

Conclusions:
These results suggest a strong relation between family resources, particularly in the areas of time and money, and parenting stress in parents of young children with autism. Increased severity of the child's symptoms was not significantly associated with parenting stress, but was associated with reports of fewer overall resources. Thus the severity of the child's autism symptoms may contribute to parenting stress via its impact on family resources, rather than directly. These results highlight the importance of developing and providing additional supports for parents of young children with autism to help them manage both the significant resource demands and the increased stress levels associated with this role. These supports may be critical for family stability as well as child outcomes.

120.06 6 Parent-Child Interaction and Global Assessment of Functioning: Measuring Change and Outcome in Adolescents with Autism. J. A. Hobson*[1], R. P. Hobson[1] and S. Gutstein[2], (1)*Institute of Child Health, UCL*, (2)*The Connections Center*

Background:

Individuals with autism have difficulties in their relations with other people – both caregivers and peers. Adolescence can bring special challenges, and co-morbid conditions may exacerbate affected adolescents' problems with adaptive functioning and quality of life. It is important to discover whether both in children and adolescents – and in given individuals across this time - these broader problems are more or less severe, depending on individuals' ability to engage with other people.

Objectives:

The objectives of this study were to investigate a) whether among children and adolescents with autism, limitations in social engagement with caregivers are associated with broader difficulties in adjustment and functioning, and b) whether *changes* in individuals' social engagement that take place from childhood to adolescence (changes that my have been fostered by the current participants' involvement in Relationship Development Intervention) correspond with *changes* in global functioning over time.

Methods:

We studied 16 families each of which included an adolescent with autism, diagnosed according to the Autism Diagnostic Observation Schedule (ADOS) and the Autism Diagnostic Interview (ADI), who had previously participated in a treatment aimed at fostering communication through parent-child and subsequently child-peer interactions.

The principal measures were of two kinds, each of which was administered when the individuals with autism were in childhood or early adolescence (chronological age = 7 years, range 2 - 13 years) and then later in adolescence (chronological age *M* = 13 years, range 10 - 17 years: time span between measures for individuals *M* = 5 years, range 3 – 8 years):

a) Interactions between the children/adolescents and their parents. There were two forms of assessment: firstly, videotape analysis of interactions using the Dyadic Coding

Scale (Humber & Moss, 2005), and secondly, caregiver-report measures.

b) Clinical judgments on the Children's Global Assessment Scale (C-GAS). These ratings were made by clinicians 'blind' to the time that data were collected, taking into account a comprehensive set of measures including formal assessments of cognitive ability, emotional and behavioral symptoms (BASC), adaptive functioning (VABS), clinical features of autism (ADOS and ADI-R).

Results:

Preliminary results suggest that in this sample, caregiver-child relatedness improved over time. This will enable us to determine whether such changes – as well as separate analyses of data at the two time-points of data collection – correspond with global measures on the CGAS.

Conclusions:

Whatever the outcome of this study, it will illustrate the value of methodologically novel approaches to the measurement of change and functioning among individuals with autism – especially in their relations with caregivers – from childhood into adolescence. It will also provide suggestive evidence on the significance of affected individuals' capacities to engage with caregivers for broader aspects of their functioning.

120.07 7 The Transition out of High School for Individuals with Autism Spectrum Disorders and Their Mothers: The Role of Age at Exit. J. L. Taylor*[1] and M. M. Seltzer[2], (1)*Vanderbilt Kennedy Center*, (2)*Waisman Center, University of Wisconsin-Madison*

Background: There is considerable variability in the age at which adolescents and young adults with autism spectrum disorders (ASD) exit the school system. Some exit with their same-aged peers, while others take advantage of the IDEA and remain in secondary school until their 22nd birthday. Little is known about the role of timing of high school exit for families of individuals with ASD.

Objectives: This study examines whether age at high school exit can be predicted from characteristics of the individuals with ASD, and whether age at exit is related to the mother-child relationship and maternal well-being.

Methods: Participants were 82 mothers with a son or daughter with ASD who exited high school prior to or during the study period. Mothers participated in five assessments over a 10-year period. Individuals with ASD in this sample averaged 16 years of age at the start of the study, with a range from 10 years to 22 years. They were 78% male, and 57% had received an intellectual disability (ID) diagnosis. The present analysis used measures of the behaviors and symptoms of the individual with ASD measured at the first assessment, including autism symptoms, maladaptive behaviors, and an indicator of whether the son or daughter had ever been diagnosed with ID. Measures of maternal well-being and the mother-child relationship for the present analysis were collected at the fifth assessment, and included depressive symptoms, anxiety, and mother-child relationship closeness.

Results: In all analyses, we controlled for the son or daughter's gender and age at the start of the study. Whether the individual had a diagnosis of ID was significantly related to age at high school exit, $F(1, 81)=49.92$, $p<.001$, accounting for 36% of the variance of age at exit. On average, those without ID exited at 19.2 years of age, and those with ID exited 1.6 years later. In addition to this main effect, ID diagnosis interacted with severity of asocial behavior problems to predict age at exit, $\beta=1.63$, $p < .05$. For those who had a comorbid diagnosis of ID, more asocial behavior problems (characterized by offensive or uncooperative behavior) were related to older age at high school exit. In contrast, asocial behavior problems were unrelated to age at high school exit for those without ID. Severity of autism symptoms was not related to age at exit. We next examined whether age at exit predicted subsequent maternal well-being (depression, anxiety) or mother-child relationship quality. After controlling for ID, gender, and age at study start, older age at exit predicted a closer mother-child relationship, $\beta = .28$, $p < .05$.

Conclusions: There was variation in the age at which individuals with ASD left the school system, with comorbid ID and asocial behavior problems explaining significant amounts of this variance. Timing of exit was not related to maternal well-being, but did predict mothers' closeness with their son or daughter. Discussion will focus on implications for transition and post-transition services.

120.08 8 Imitation Skills Predict Subsequent Language Gains in Children with Autism. N. Crane*[1], M. Siller[1], M. Sigman[2] and T. Hutman[2], (1)*Hunter College of the City University of New York*, (2)*University of California, Los Angeles*

Background: A variety of authors have reported that children with autism show specific deficits in imitation skills (Rogers, Hepburn, Stackhouse and Wehner, 2003). Moreover, individual differences in imitation were shown to predict subsequent gains in language, even if even if initial child characteristics (language age, IQ) were statistically controlled (Stone & Yoder, 2001, Charman, 2003, Toth, Munson, Meltzoff and Dawson 2006).

Objectives: In this longitudinal study, we administered a comprehensive imitation battery that evaluates four types of imitative behaviors: manual, object, oral-motor and verbal (Rogers, Hepburn, Stackhouse and Wehner, 2003). We aimed to evaluate predictive relations between these four types of imitative behaviors and children's subsequent gains in language skills.

Methods: The sample consisted of 34 individuals with autism (chronological age: mean = 55.9 months; SD = 11.9 months), who participated in the control condition of a randomized controlled intervention trial. At baseline, children were administered the imitation battery. A total of 24 imitation probes were administered over the course of 2 lab visits, with 5-7 tasks in each category. In addition, we evaluated children's receptive and expressive language abilities using the Mullen Scale of Early Learning (Mullen, 1995). Children's language abilities were also measured during two waves of follow-up assessments, scheduled 6 and 18 months after the baseline assessments were completed. The imitation tasks were videotaped; coders later reviewed these videos and decided whether the children correctly imitated the target behaviors or not (i.e., pass, fail). Inter-observer reliability was established between two independent observers (ICC scores ranged between .97 to .98).

Results: Results revealed significant correlations between all four measures of imitation skills and children's expressive/receptive language skills at follow up (waves 2 and 3). However once initial language skills and chronological age were statistically controlled, only some of these correlations remained significant. That is, partial correlations revealed significant correlations between children's verbal imitation scores and their receptive language scores at wave 2 (partial-r=.486, $p<0.05$) and wave 3 (partial-r=.396 $p<0.05$); similarly, a significant partial correlation was found between object imitation and children's expressive language skills at wave 3 (partial-r=.439, $p<0.05$). Finally, oral-motor imitation skills predicted both receptive (partial-r=.512, $p<0.01$) and expressive (partial-r=.393, $p<0.05$) language skills at wave 2.

Conclusions: This research reveals a complex pattern of relations between different domains of imitative behavior and children's subsequent language gains. The ability to imitate spoken words appears to predict gains in a child's ability to understand and respond to language, but not necessarily their ability to produce spoken language. The opposite is true for a child's ability to imitate object manipulations. Only oral-motor imitation skills appeared to predict both expressive and receptive language gains.

Support: This research was supported by CPEA Grant HD-DCD35470; the M.I.N.D. Institute Research Program; an Autism SPEAKS Early Intervention & Treatment Grant.

120.09 9 Longitudinal Rasch Analysis of Imitation in Infants at Risk for Autism. G. S. Young*[1], S. J. Rogers[2], M. Sigman[3], T. Hutman[3], W. Mattson[2], J. Martinez[2] and S. Ozonoff[1], (1)*M.I.N.D. Institute, University of California at Davis Medical Center*, (2)*M.I.N.D. Institute, University of California at Davis*, (3)*University of California, Los Angeles*

Background: Imitation is significantly impaired in children with autism compared to other groups, and may be an early central feature of the disorder. However, few studies have examined the development of imitation prior to formal diagnosis, and studies are often hampered by the lack of a standardized developmental measure of imitation.

Objectives: We aimed to test whether individual differences in imitation ability during the second year of life would predict ASD diagnoses at 3 years of age. A second objective was to use Rasch analysis to evaluate the psychometrics of a standardized imitation battery, and to explore the Rasch model as a multi-level longitudinal logistic regression model to test developmental trajectories in imitation over time as a function of clinical outcomes.

Methods: One hundred forty-six infant siblings of children formally diagnosed with autism or ASD and 87 infant siblings of typically developing children were seen at 12, 18, 24 and 36 months of age. An imitation battery based on the Uzgiris

and Hunt (1975) scales of imitation was given at 12, 18, and 24 months, and clinical outcomes were measured at 36 months of age. Outcome classifications consisted of autism/ASD (n=20), typically developing (n=158), and other clinical concerns (n=55). The imitation scale, consisting of ten gestural imitation items, was administered and scored on a 3-point scale – pass, partial-pass, fail. Item scores were analyzed using a partial-credit Rasch model to estimate item difficulties, differential item functioning across time, and response category thresholds. A longitudinal multilevel Rasch model was fit to dichotomized scores to evaluate group differences in change over time.

Results: Rasch analysis of item data suggested that all 10 items showed adequate fit using mean-square and infit statisistics.. Analysis of item data across and within the 3 ages revealed good item separation and item reliability and acceptable person separation and reliability. Examination of category thresholds revealed that items were best represented as dichotomous data. Analysis of differential item functioning between ages suggested good scale stability of item difficulty estimates. A multi-level longitudinal logistic regression with item scores modeled at level-1 confirmed Rasch item scaling and further showed main effects of outcome group and age, as well as an outcome group by age interaction (Wald X^2 = 6.48, df = 2, $p < .05$), with typical infants showing the greatest growth over time compared to other groups. Group comparisons at each time point revealed that although typical subjects were significantly better than both the ASD and other clinical groups by 18 and 24 months, imitation performance did not differ between the ASD and other clinical groups.

Conclusions: Findings illustrate the use of Rasch analysis to evaluate an imitation test battery, and to model growth over time as a function of outcome. Early deficits in imitation differentiate infants with autism from typically developing infants by 18 months, but not from those with other clinical concerns.

120.10 10 Does Family Affectedness Predict Outcomes in Infants at Risk for Autism?. A. J. Schwichtenberg*[1], S. Ozonoff[1], S. J. Rogers[2], M. B. Steinfeld[1], G. S. Young[1] and M. Moore[1], (1)*M.I.N.D. Institute, University of California at Davis Medical Center*, (2)*M.I.N.D. Institute, University of California at Davis*

Background: Infant siblings of children with an autism spectrum disorder (ASD) are more likely to develop an ASD when compared to siblings of typically developing children (e.g., Landa, Holman, & Garrett-Mayer, 2007). Although the mechanisms for this risk are largely unknown, genetic factors are often implicated. The broader autism phenotype (BAP) is a constellation of subclinical behaviors associated with ASD that can be found in non-autistic family members. The BAP includes differences in social interactions, relationships, communication skills, and restricted patterns of behavior or intense interests. The BAP is thought to be an index of family genetic risk for autism (Piven, 2001).

Objectives: Within this study, the presence of ASD and BAP in family members or 'family affectedness' is explored as a predictor of infants developing an ASD, BAP behaviors or other developmental concerns.

Methods: As part of a larger longitudinal study, these analyses included seventy-five infant siblings from families raising one child (simplex families; *n* = 68) or more than one child (multiplex families; *n* = 7) with an ASD. At 24 or 36 months of age the enrolled infant siblings were categorized as typically developing (56%), with an ASD (12%), with behaviors consistent with the social deficits of the BAP (16%), or other developmental concerns (16%). Family affectedness was conceptualized as the number of first degree family members with either an ASD or the social/communication features associated with the BAP (as measured by the Social Responsiveness Scale). Approximately 12% of fathers, 13% of mothers, 9% of male siblings, and 11% of female siblings had social/communication differences consistent with the BAP.

Results: Regression analyses assessed if a family history of ASD and/or BAP behaviors could predict which infant siblings would themselves develop an ASD, BAP behaviors, or other developmental concerns (while controlling for family size). Paternal social/communication deficits and family size predicted the occurrence of multiplex families, which, in turn predicted which infant siblings would develop an ASD. In this study, infant siblings from multiplex families were seven times more likely to develop an ASD than infant siblings from simplex families. Family size predicted the frequency of BAP and other

developmental concerns, such that larger families had more members with BAP behaviors or other developmental concerns.

Conclusions: Broader phenotype features in fathers were more common in multiplex families and infants of multiplex families were more likely to develop an ASD. This research suggests that early monitoring and intervention services designed for this at-risk population should assess and support family social/communication skills to identify infants at elevated risk and to promote optimal parent-child interactions - the proximal context for child development.

120.11 11 Patterns of Changes in Development in Children with Autism Compared to Typically Developing Children. L. D. Swensen[1], D. Fein[2] and L. Naigles*[2], (1)*NYS Institute for Basic Research in Developmental Disabilities*, (2)*University of Connecticut*

Background: Vocabulary and grammatical development in children with autism has been compared to typically developing children. For vocabulary acquisition, children with autism appear delayed in their acquisition of vocabulary, but it does increase over time (Dunn & Rapin, 1997). For grammatical complexity, it appears that at smaller MLUs (i.e. earlier in development) there may be very little difference between autistic and normal children in terms of the relationship between utterance length and grammatical complexity; however, when MLU exceeded 3.0 significant differences arose (Scarborough et al, 1991). That is, ASD children did not add grammatical complexity to their longer sentences like the typical children.

Objectives: The current study addressed patterns of change in vocabulary, sentence length, as well as socialization skills, which have long been understood to be a contributing factor in language growth (Mundy, Sigman, & Kasari, 1994).

Methods: 10 boys with Autism Spectrum Disorder (ASD) and 10 typically developing children (TYP) (four boys and six girls) participated in a longitudinal study. At Visits 1-4, carried out every four months (ASD: 33-45 months old; TYP: 17-29 months old), the mother-child dyads participated in 15-minute free play sessions, which were transcribed and analyzed. Standardized tests were also administered. The two groups were matched on language variables at visits 2 and 3. Four variables were analyzed to inspect patterns of change: number of word types in spontaneous speech, MLU in spontaneous speech, CDI scores, and Vineland Adaptive Behaviors Scales Socialization scores. Analyses of change over time, group differences, and their interaction were conducted using a Multilevel Model of Change in SPSS.

Results: For the three language variables, significant main effects of both time and group, as well as group by time interactions emerged (*ps*<.002). The group differences demonstrated a difference in initial status of the two groups, which confirmed by t-tests, with the ASD group scoring higher. A significant main effect of time showed that both groups increased their scores on each of the variables over time. A significant interaction between group and time emerged, with the TYP group having a steeper trajectory on all three variables. For the VABS socialization scores, no significant group effect emerged. A significant effect of time emerged (*p*<.001), demonstrating that both groups increased their socialization scores across visits. The interaction between time and group was not significant, in that the pattern of change in socialization scores across time was not significantly different for the two groups.

Conclusions: The language measures revealed significant differences in the pattern of change for the two groups, which was to be expected from prior research. A difference in the pattern of change in socialization for the two groups was expected due to the close tie between socialization and language. Some have suggested that problems with the form of the language may stem from difficulties in understanding the function of communication. The findings of this study may contradict these findings, in that for that this group of ASD children there was a disconnection between the growth of language and socialization skills.

120.12 12 Outcomes in Young Children with Autism and Developmental Delay: Behaviour and Emotional Problems and Autism Symptomatology. K. M. Gray*[1], B. J. Tonge[1], D. J. Sweeney[1] and S. Einfeld[2], (1)*Monash University*, (2)*University of Sydney*

Background: Research indicates that there are high levels of behaviour problems present in young children with developmental delay, particularly in young children with autism. These behaviour problems are a significant contributor to parental psychosocial distress.

Objectives: To explore the presentation and the course of child behaviour problems and autism symptomatology over time. To determine if early markers of cognitive, social, and communication skills in young children are associated with subsequent behavioural outcomes.
Methods: One-hundred and eighty-seven children with developmental delay were followed-up 2 years after their initial assessment and diagnosis. At initial assessment the children were aged 20-55 months, and approximately two-thirds received a diagnosis of a Pervasive Developmental Disorder. Information on symptomatology, behaviour problems, developmental level, expressive and receptive language ability, adaptive behaviour, parent mental health, stress and family functioning was collected at both time points.
Results: Data will be presented on the course of autism symptomatology and behaviour problems over time in young children with developmental delay compared to young children with autism. Associations with developmental course and language development will also be explored.
Conclusions: As research has shown that behavioural and emotional problems in autism persist into adolescence and young adulthood, greater understanding of these issues in very young children will have implications for intervention and long term outcome.

120.13 13 Social and Communicative Deficits in the First Year of Life; Prediction of Later Diagnosis. S. Schjolberg*, *Norwegian Institute of Public Health*

Background:

Autism is a behavioural, developmental disorder characterized by abnormal social interaction, disordered communication and lack of imaginative play. It is regarded as the most severe psychiatric disorder in childhood, but is rarely diagnosed before 3 years despite the fact that the majority of cases have a symptom onset during infancy.
A diagnosis of autism is generally based on information derived from both parental reports and clinical observation. However certain key behaviours may not readily be observed in a clinical setting during a brief and highly structured visit. It is therefore of importance to identify which behavioural features that reliably can be describe by the parents and that are of relevance for an early diagnosis of autism.

Objectives:

Explore whether most parents of children with a suspected autismspectrumdisorder (ASD) report similar developmental concerns the first year of life? Explore whether parents of children with ASD report different types of early concerns than parents of children with other developmental problems?

Methods:

The sample consists of 94 children (75 boys, 19 girls) consecutive referred for suspected autism spectrum disorders. Mean chronological age is 6,8 years (SD 3,1). At referral parents are asked to rate their child's current behaviour. In addition they are asked to retrospectively rate their child's behaviour before their second birthday. Both the children's social and communicative competencies as well as presence of abnormality in the first two years were rated. Forty parents were asked to complete the checklists twice for test-retest of information.

Results:

The parent's early concerns about their child's early development are reported. Behaviour features reported the first two years in life are used to predict later development. Discriminant analysis is used to identify the behavioural features that best predicts the child's diagnostic status.

Conclusions:

No single behavioural feature is unique for ASD in early development. A combination of behavioural features reported earlier than two years of age seemed to best predict a diagnosis within the autismspectrum.

120.14 14 Academic Outcomes of Youth with Autism. J. Kurth*[1] and A. M. Mastergeorge[2], (1)*Northern Arizona University*, (2)*M.I.N.D. Institute, University of California at Davis*

Background:

The increasing prevalence of autism, along with legal and philosophical rationales for inclusion in general education, necessitates determining if inclusive education benefits youth with autism. It is important to understand the academic ability of youth with autism and the impact of inclusion in general education on academic development.
Objectives:

The following research questions are addressed: (1) what are the academic strengths and weaknesses of adolescents with autism? (2) What are the educational goals, services, and needs for youth with autism, and do these change over time? (3) Does placement in inclusion versus non-inclusion impact academic goals, achievement, and engagement?

Methods:

Fifteen students with autism between the ages of 12 and 16 years participated in this study. All students were continuously enrolled in special education inclusion or non-inclusion settings. Three measures were used: records review, assessment, and observation. First, cumulative IEP records were analyzed for type of goal, goal progress, services, and accommodations. Second, students were assessed using the Vineland Adaptive Behavior Scales, the Woodcock-Johnson III Tests of Achievement (WJ-3), and the Wechsler Intelligence Scale for Children (WISC) or the Test of Non-Verbal Intelligence (TONI). Finally, students were observed in their math and language arts classes to note their levels of engagement, learning partners, curriculum use, instructional activities, and location of instruction. The engagement patterns of adolescents with autism were compared to the engagement patterns of other students in the class.

Results:

Records Review: All students with autism had a large number of IEP goals and limited progress in meeting their IEP goals. Students who are included have goals derived from higher content standards, have more goals addressing higher order thinking and problem solving skills, and were more likely to meet their annual IEP goals. Services varied by program as well, with older students having more "managerial" services and younger students with more "remedial" services. Students who are included had more accommodations.
Assessment: Students in both programs had statistically non-significant intelligence and adaptive behavior scores. However, the students who were included had statistically significant higher academic achievement as measured in all three sub-tests of the WJ-3. All students had relative strengths in rote, memory-based academic skills, but those students who are included had statistically higher scores on all sub-tests areas.
Observation: Students who are included were accessing the core curriculum, had more teacher directed instruction, completed more independent work, and were more passively engaged.
Students with autism who were not included in general education completed more individual instruction, used alternate curriculum, were primarily instructed by paraeducators, and were more actively engaged. Students who were not included had a high frequency of breaks during instructional time (approximately 30% of their instructional time).
Conclusions:

These findings indicate the value of academic inclusion for students with autism in general education. We find that inclusion is associated with greater academic achievement and participation in the core curriculum, the development of higher-order thinking skills, access to higher grade level content standards, and more accommodations and services provided to individual students.

120.15 15 The Effect of Age and IQ on the Acquisition of Adaptive Skills in Girls with Autism. K. A. Loveland*[1], D. A. Pearson[1] and T. CPEA/STAART Girls with Autism Study Group[2], (1)*University of Texas Medical School at Houston*, (2)*N/a*

Background: Previous studies have demonstrated that many children with autism plateau with respect to the acquisition of new adaptive functioning skills during the adolescent years. However, the influence of gender on the trajectory of adaptive skill development in autism is not well understood. We earlier reported that IQ was a better predictor of adaptive standard score (SS) in girls than boys with autism, but that age was not related to adaptive SS in either group. Objectives: The purpose of this study was to extend previous findings by examining the relationship of age and IQ to absolute level of adaptive development (raw scores) in our cross-sectional sample of girls with autism. Methods: Participants were 94 females with autism (mean age=7.5 yrs; mean VIQ=64) who met DSM-IV criteria for an autism spectrum disorder on the ADI-R and the ADOS. Primary caregivers (usually the mother) were interviewed using the Vineland Adaptive Behavior Scales at 17 contributing CPEA and/or STAART centers. IQs were obtained using age appropriate standardized measures. Multiple regression was performed with Verbal IQ,

Nonverbal IQ and Chronological Age entered simultaneously into the model as predictors of the major domain raw scores.
Results: Both Verbal IQ (p = .000) and Chronological Age (p = .000) were found to be positively related to all three major Vineland domain raw scores, Communication, Daily Living and Socialization, however Nonverbal IQ was not significant in any of the three models.
Conclusions: These results indicate that in this sample of girls with autism, greater age was associated with greater absolute level of adaptive skills in all three domains examined, even with effects of Verbal and Nonverbal IQ controlled. This finding suggests that not all children with autism may plateau in acquiring adaptive skills. Because this sample was cross-sectional, however, further research should examine trajectories of adaptive development longitudinally across the development of girls with autism.

120.16 16 Environmental Pollutants and Markers of Autoimmunity as Risk Factors for Autism Spectrum Disorders in California's Central Valley. K. Cheslack-Postava*[1], J. K. Grether[2], E. Roberts[2], G. C. Windham[2] and C. Newschaffer[3], (1)*Columbia University*, (2)*California Department of Public Health*, (3)*Drexel University School of Public Health*

Background: The etiology of autism spectrum disorders (ASD) appears to be influenced by a complex set of genetic and environmental factors, which may be interacting with each other to determine risk. While life in the modern industrialized world involves exposure to myriad chemicals and pollutants on a daily basis, few of these have been well-studied with respect to ASD. Current evidence suggests a relationship between autoimmunity and ASD; chemical exposures that effect autoimmunity may exacerbate any such relationship.
Objectives: To assess potential interactions between selected chemical exposures and neonatal levels of autoantibodies in association with risk of autism spectrum disorders.
Methods: We measured IgG autoantibodies to nervous system and thyroid antigens in neonatal blood spots from ASD cases (N=384) identified through the California Department of Developmental Services and population controls (N=596) born between 1996 and 1998 in California's Central Valley. Estimates of ambient levels of hazardous air pollutants (HAPs) and measures of regional pesticide applications were derived through linkage to existing databases, based on mother's residence at the time of delivery. Interactions between exposures and autoantibodies were explored using logistic regression models to calculate odds ratios (ORs) for ASD risk adjusted for demographic and birth characteristics. A total of 228 autoantibody-chemical combinations were tested in exploratory models including interaction terms; autoantibody-ASD ORs, stratified by exposure level, were computed based on significant p-values for tests of interaction. Associations of these chemical exposures with ASD risk and associations between exposure and autoantibodies were also explored.
Results: We previously observed inverse associations between autoantibody levels and odds of ASD in this sample. Consistent with this, GFAP and MBP autoantibody levels above the 95th percentile were associated with significantly reduced odds of ASD in the lower exposure categories (quartiles 1-3 for HAPs) of chemical groups including immunotoxicants, neurotoxicants, and chlorinated solvents. However, in the higher exposure categories (quartile 4) of these chemical groups, ORs for ASD and GFAP and MBP autoantibody levels above the 95th percentile were associated with increased risk for ASD. For example, where chlorinated solvent levels fell in the lower three quartiles, the OR for ASD-MBP autoantibody association was 0.33 (95% CI (0.14, 0.80)); for the 4th quartile of exposure, the OR for ASD-MBP autoantibodies was 2.80 (95% CI (0.60, 13.1)). Other findings included associations of both chlorinated solvents in ambient air and organochlorine pesticides with levels of thyroid peroxidase antibodies above the 95th percentile (OR (95% CI) = 3.0 (1.02, 8.79) and OR (95% CI) = 7.23 (1.57, 33.2), respectively).
Conclusions: Exposure to environmental pollutants may modify associations between autoantibodies and ASD. This could indicate that additional immunologically active stimuli are required to potentiate autoantibody-mediated processes involved in ASD etiology. However, as these were exploratory models comparing multiple exposure-autoantibody combinations, further research will be required to fully understand these complex relationships. Funding sources**:** Autism Speaks and the California Department of Public Health

120.17 17 Chemicals That Interact with Autism Gene Candidates. M. A. Corrales*, *US Environmental Protection Agency*

Background:
Although epidemiologists and toxicologists have started to investigate several chemicals as

potential autism risk factors, it is still unclear what chemicals should be studied in this regard. A more objective and comprehensive approach to screening and prioritizing chemicals would be useful in designing future studies. This work should be informed by the most recent findings in the genetics of autism.
Objectives:
This analysis was an effort to find and demonstrate a way to cast a relatively wide net to identify chemicals that might merit further investigation as potential risk factors in autism, drawing upon the full range of genetic findings and a wide range of literature on gene-chemical interactions.
Methods:
The Comparative Toxicogenomics Database (CTD, http://ctd.mdibl.org) and AutDB (http://www.mindspec.org) were selected as relatively comprehensive, powerful tools for this type of analysis. The AutDB was used to identify 142 genes (as of late 2008) studied in autism, of which 122 genes were found to have reported chemical interaction data in the CTD. These interactions often consist of observed changes in gene expression in rodents exposed to various levels of the studied chemical substance. The chemical-gene interactions, GO terms, and pathways associated with these genes in the CTD were analyzed, and chemicals were manually classified as xenobiotics, medications, nutrients, and endogenous substances. Chemicals were prioritized based on number of reported interactions.
Results:
The genes MET, PTEN, ADRB2, and TH each had more than 30 interacting chemicals identified in the CTD, and 120 chemicals were reported to interact with PON1. Other genes, such as MECP2, TSC2, RELN, UBE3A, and GABRB3, showed interaction reports for only 4-14 chemicals each in the CTD. For many genes, such as EN2, SHANK3, FMR1, NLGN3, and NRXN1, the CTD contains interaction reports for only 1-2 chemicals so far. Over 600 chemical substances were identified as interacting with any of the 122 autism candidate genes, of which 498 had unique CAS numbers. Xenobiotics (or closely related substances) identified as interacting with autism candidate genes included the following (# of genes in parentheses): Carbon Tetrachloride (33), tert-Butylhydroperoxide (19), sodium arsenite (17), Lipopolysaccharides (11), Paraquat (10), nickel sulfate (9), Hydrogen Peroxide (9), arsenic trioxide (8), Benzene (7), Benzo(a)pyrene (7), Ethanol (7), Tobacco Smoke Pollution (4), Arsenic (4), Chlorpyrifos (4), Tetrachlorodibenzodioxin (4), and bisphenol A (4). Other chemicals previously implicated in autism or related conditions are also identified by this analysis, such as mercury compounds, lead, cocaine, fipronil, endosulfan, and phthalates.
Top substances related to dietary nutrients: Pirinixic acid (27 genes), Zinc, Resveratrol, Flavonoids, and Dietary Fats.
Top medications: Acetaminophen (49 genes), Tamoxifen, Diethylstilbestrol, Valproic Acid, and Celecoxib.
Top endogenous (or closely related) substances interacting with numerous autism candidate genes: Progesterone (37 genes), Estradiol, Ethinyl Estradiol, Corticosterone, and Thyroxine.
Conclusions:
As bioinformatics databases grow, they can inform prioritization of candidate environmental risk factors.

120.18 18 Impact of Family History of Depression on Cognitive Ability and Symptom Severity in Autism. R. A. Barry* and E. M. Griffith, *University of Alabama at Birmingham*

Background: A link has been found between autism spectrum disorders and an increased amount of familial mood disorders. Moreover, in an as yet unexplained set of findings, a possible link exists between familial depression and increased cognitive ability in autism.

Objectives: The purpose of this study, in addition to replicating previous studies in a larger sample, will be to examine the possible explanations for the link between depression in families and increased cognitive abilities in autism by investigating the correlation between specific diagnosis on the autism spectrum (autistic disorder vs. Aspergers vs. PDD) and familial depression, as well as between symptom severity and familial depression.

Methods: Archival data collected in the course of clinical diagnostic evaluations for individuals diagnosed with an autism spectrum disorder will be examined.

Results: Pilot data has been analyzed. An ANOVA revealed a trend for IQ being higher in the group with a family history of depression, approaching significance, $F(1,24) = 3.50$, $p=0.074$. Further analysis showed that the participants were equally represented each autism spectrum disorder, and

that there was no significant difference in symptom severity of those with and without familial history.

Conclusions: Pilot analyses support previous findings of higher mean IQ for participants with an ASD who have a family history of depression than for those without. The results also imply that the difference in IQ cannot be attributed to differences in group membership and symptom severity.

120.20 20 Pro- and Anti- Saccade Abnormalities in First-Degree Relatives of Individuals with Autism. M. W. Mosconi*, A. M. D'Cruz, M. Kay, L. Ankeny, L. D. Stanford and J. A. Sweeney, *University of Illinois at Chicago*

Background: Saccades are rapid eye movements that shift the focus of gaze. Cortico-cerebellar feedback loops modulate the accuracy of saccades and control for motor error. Inhibitory control of reflexive saccades engages fronto-striatal pathways and can be assessed using anti-saccade tasks in which participants make saccades away from targets presented in their visual field. Decreased accuracy of saccades and poor inhibitory control (i.e. increased rates of saccades made *towards* instead of away from targets) on anti-saccade tasks have been observed in individuals with autism. These deficits and their underlying pathophysiology could serve as useful intermediate phenotypes, but saccade performance has not yet been systematically investigated in unaffected family members of individuals with autism.

Objectives: To investigate sensorimotor and cognitive control of saccades in first-degree relatives of individuals with autism.

Methods: Fifty-nine first-degree relatives (parents and siblings) of individuals with autism and 31 age- and IQ-matched healthy control individuals between 8-55 years of age performed visually guided pro-saccade and anti-saccade tasks. During the prosaccade task, participants made reflexive saccades to peripheral targets. During the antisaccade task, participants were instructed to inhibit saccades towards novel peripheral targets and instead make a saccade to the mirror location of the target. Each task included gap and overlap conditions. 'Gap' trials were characterized by extinction of a cross-hair at central fixation 200 ms *prior* to presentation of a peripheral stimulus. 'Overlap' trials were characterized by extinction of a cross-hair at central fixation 200 ms *after* presentation of a peripheral stimulus. The latency and accuracy of prosaccades were examined. Anti-saccade error rates (the failure to inhibit prepotent responses) and latency of anti-saccades were examined.

Results: Saccades of family members during the prosaccade task were less accurate and more variable in their accuracy than those of controls during gap trials only. Family members also made more anti-saccade errors than controls in the gap condition. No group differences in the latency or peak velocity of pro- or anti-saccades were observed in any task.

Conclusions: First-degree relatives of individuals with autism show impairments in sensorimotor and inhibitory control of saccades that parallel those previously observed in probands. The saccadic dysmetria and poor inhibitory control of reflexive saccades observed in family members implicate cerebellar circuitry involved in fine motor control and frontostriatal circuitry critical to the top-down control of motor behavior. These findings in unaffected family members suggest that disturbances within these neural systems may be useful intermediate phenotypes for research into the genetic bases of autism.

120.21 21 Procedural Learning Abnormalities in First-Degree Relatives of Individuals with Autism. M. W. Mosconi*, K. Kapur, A. M. D'Cruz, L. Ankeny, M. Kay, L. D. Stanford and J. A. Sweeney, *University of Illinois at Chicago*

Background: Procedural learning involves the implicit learning of simple behavioral response patterns through repeated practice. Individuals with autism have impaired performance on complex serial response learning tasks involving manual responses, and an altered ability to time predictive responses during an oculomotor serial reaction time task.

Objectives: To investigate procedural learning during a predictive saccade task of procedural learning in first-degree relatives of individuals with autism.

Methods: Fifty-one first-degree relatives (parents and siblings) of individuals with autism and 37 age- and IQ-matched healthy control individuals between 8-54 years of age performed an oculomotor predictive saccade task and a sensorimotor control task. During the predictive saccade task, participants looked at a light that shifted position back and forth between locations

6 degrees of visual angle to the left and right of central fixation every 750 ms seconds for 40 trials. A visually guided saccade (VGS) control task was administered in which saccades to unpredictable targets were examined. The latency of saccades was examined in each eye movement task.

Results: The timing of saccades to unpredictable targets was not altered in the unaffected family members. In the predictive saccade task, family members' rate of learning to speed their responses to predictable target appearance was slower than that of healthy controls. Further, their response latencies remained slow after learning asymptote had been achieved.

Conclusions: First-degree relatives of individuals with autism show decreased rates of procedural learning on an oculomotor serial reaction time task, and they are not able to respond as rapidly as controls once they achieve peak performance. This pattern of findings likely reflects alterations in frontostriatal systems. The demonstration of reduced procedural learning capacity in unaffected family members of individuals with autism suggests that this deficit may serve as a useful endophenotype for family genetic research.

120.22 22 Linguistic Markers of Genetic Liabitiy to Autism. M. Losh* and P. C. Gordon, *University of North Carolina at Chapel Hill*

Background: Deficits in language discourse (i.e., connected speech such as conversation and narrative) are a hallmark of autism, and a principal feature of the broad autism phenotype, or BAP -- i.e., the constellation of subtle features often observed in relatives of autistic individuals that are qualitatively similar to the core features of autism and are believed to index genetic liability to autism. While existing clinically-based measures of discourse have provided highly valid and richly descriptive information, the vast majority of such measures tend to assess behavior at a functional rather than mechanistic level. Thus, relatively little is known regarding the underlying cognitive mechanisms that give rise to observed discourse abnormalities, and importantly, whether such mechanisms are impaired in both in both autism and the BAP.

Objectives: This project aimed to clarify the mechanisms underlying discourse impairments in autism and the BAP, which may index genetic liability and be useful for genetic studies. We performed computational linguistic analyses to examine the relative frequency of different classes of words as a measure of psychological processes underlying discourse practices. The use of certain classes of words provides a powerful implicit measure of important psychological processes. This is particularly so for classes of words (e.g., pronouns and articles), which are essential to establishing a referential model of the meaning of a discourse exchange. While impaired processing of linguistic reference has been described in autism, no systematic research has been conducted on autism or the BAP in parents using the comprehensive tools for studying word usage applied in this study.

Methods: The frequency of different word classes was examined in existing language corpora using a computerized tool called *Linguistic Inquiry and Word Count*, or LIWC (Pennebaker et al., 2001). LIWC was designed to analyze psychological characteristics of individuals, and social characteristics of interactions, using samples of natural language (either written language or transcripts of spoken language). LIWC was applied to transcripts of discourse produced during the semi-structured interviews with 28 high-functioning individuals with autism and 23 age and IQ-matched controls, as well as transcripts of comparable language samples from 15 autism parents who had been clinically rated as BAP (+) using established methods, and 11 parents rated as BAP (-).

Results: Specific patterns of word usage were detected in both individuals with autism and parents with the BAP. Specifically, pronouns and other devices used to create coherence in discourse, discriminated individuals with autism from controls (p values $< .05$) and parents with the BAP from parents without the BAP ($p < .01$). Discriminant function analysis was conducted using these linguistic measures as predictors of autism, and the clinically-based BAP classification of the parents. Analyses correctly classified 92% of children and 84.6% of parents.

Conclusions: Findings indicate specific patterns of word class usage that may underlie the discourse abnormalities associated with autism and the BAP. These features appear to serve as markers capable of defining with strong sensitivity individuals with autism and parents with the BAP.

120.23 23 A Behavioral Genetics Study of Autism, NJLAGS. Z. Fermano*[1], J. Flax[1], B. Zimmerman-Bier[2] and L. Brzustowicz[1],

(1)*Rutgers University*, (2)*UMDNJ - New Jersey Medical School*

Background: The New Jersey Language and Autism Genetics Study (NJLAGS) is an ongoing innovative study that combines comprehensive genetic analyses with an extensive evaluation of the oral language, reading, social, and behavioral profiles of families who have at least one member who meets criteria for an autism spectrum disorder (ASD) and at least one other family member who meets criteria for a specific language impairment (SLI). There are research groups who have examined the language patterns of individuals with ASD in relation to the language profiles of individuals with SLI and found striking similarities (Condouris, Smith, Arin, & Tager-Flusberg, 2001, 2004; Conti Ramsden, Simkin, & Botting, 2006; Whitehouse, 2008). NJLAGS extends this line of research to first and second degree relatives of ascertained ASD and SLI probands and combines it with the current work of geneticists who are examining linkage and candidate genes for both disorders (Alarcon, et al., 2004, 2008; Bartlett, et al., 2002, 2004; Brune, et al., 2007; Bradford, et al., 2001).

Objectives: As in introduction to the study, we will present NJLAGS in terms of its criteria for eligibility, the behavioral testing battery administered to subjects, the language phenotypes already developed, and preliminary language profiles of our ASD and SLI subjects to date.

Methods: Potential ASD probands are diagnosed using the ADI-R, the ADOS, and a comprehensive physician's examination including the DSM-IV. SLI probands are diagnosed by a licensed Speech/Language Pathologist. Once it is determined that there are two probands, the rest of the nuclear family complete a comprehensive neuropsychological battery and donate a blood sample for DNA analysis.

Results: Thus far, 381 family members have given DNA samples and have completed the entire comprehensive behavioral battery. We have identified 80 subjects who meet criteria for Autism and 16 subjects who meet criteria for ASD. Included here is a preliminary profile of their language. Based on the ADI-R, 38% produced single word utterances by 24 months while 62% either produced them later than 24 months or are still non-verbal. Twenty eight percent of our sample has achieved phrase speech by 36 months while 72% achieved this later or still have not achieved this milestone. We examined the group of higher functioning ASD probands who were able to participate in the standardized language testing that was administered to other family members. As a group, the ASD probands scored between one and two standard deviations below matched peers on all language measures with relative strengths in various forms of vocabulary knowledge and relative weaknesses in grammar, inferential language, and the pragmatic use of language. Approximately 29% of family members met criteria for SLI based on at least four different phenotypes.

Conclusions: This research is the first large genetics study to look at the connection between language-based learning problems and autism in New Jersey. Detailed descriptions of the phenotypes and affectation rates of family members will be included as well as how these phenotypes might be applied to linkage analysis and already identified candidate genes.

120.24 24 Birth Order Effects in Multiplex Autism Families. L. Waldenmaier*[1], S. Foley[1], I. Rezek[2], K. Wittemeyer[1], H. L. Hayward[3], S. Wallace[1], J. Parr[4] and A. Bailey[1], (1)*University of Oxford*, (2)*Imperial College London*, (3)*Unviversity of Oxford*, (4)*Great Ormond Street Hospital*

Background:

There have been several studies of the possible effects of birth order on IQ and ADI scores in multiplex autism families, without any clear pattern emerging. Lord (1992) and Spiker et al (2001) found decreasing Performance IQ (PIQ) with increasing birth order in 16 and 144 multiplex families respectively. Spiker et al. (2001) and Reichenberg et al. (2007) both found higher repetitive ADI domain scores in firstborns in 144 and 106 multiplex families respectively. Reichenberg et al. (2007) also found significantly more firstborns with functional and spontaneous phrase speech, but found no difference in social or non verbal communication scores in 106 families.

Objectives:

This study aims at clarifying the nature of the relationship between birth order and different domains of functioning in ASD. This research overcomes some previous methodological flaws (e.g. heterogeneous IQ tests; small sample sizes)

and extends previous research to include verbal IQ (VIQ).

Methods:

Data was collected on 480 individuals with ASD from 240 multiplex families included in the International Molecular Genetics Study of Autism Consortium (IMGSAC). All individuals with ASD received an ADI-R (Lord, C., Rutter, M., & Le Couteur, A., 1994) and several IQ tests were administered but most were Raven's Progressive Matrices (performance IQ) or Picture Vocabulary (Verbal IQ). The age at testing for the secondborns was significantly younger than firstborns at time of administration of the ADI-R and the IQ tests. The effect of age was controlled for on both performance and verbal IQ, by saving the unstandardized residuals of a regression analysis, with age as the predictor and IQ as the dependent variable. The saved unstandardized residuals of each computation were then used as variables in the paired sample t-test analysis.

Results:

There was no significant difference in PIQ between first and second born siblings when either all PIQ data were included (t=-.304, p=.761) or when the analysis was restricted to Raven's Progressive Matrices scores (t=.022, 0=.983). Neither was there any significant difference in VIQ between first and second born siblings when all tests were included (t=-1.521, p=.132) or when only Picture Vocabulary data were analysed (t=.482, 0=.631).

Conclusions:

Once the effect of age of administration was controlled for, there was no significant difference in performance or verbal IQ between first and second born individuals in multiplex autism families.

120.26 26 Agreement Between ADI-R and ADOS in a Twin Sample. N. Gillan*[1], E. Woodcock[1], V. J. Hallett[1], C. Ames[1], E. Colvert[1], F. Happé[1] and P. Bolton[2], (1)*Institute of Psychiatry, KCL*, (2)*Institute of Psychiatry*

Background:

Clinical best practice in the diagnosis of ASD calls for use of standardized measures of both parent report and clinical observation of interaction. The ADOS and ADI-R are currently considered gold-standard measures in this capacity. However, disagreement between these instruments is not uncommon. Understanding the likely sources of disagreement between parental report and clinical observation is important for both clinicians and researchers.

Objectives:

This study explores possible sources of disagreement between parental report (from ADI-R) and clinical observation (ADOS), by contrasting data from MZ and DZ twins.

Methods:

Data is being collected as part of the Social Relationships Study (SRS), a twin study of the full autism spectrum embedded within the Twins Early Development Study (TEDS). The SRS study includes MZ and DZ twin pairs in which one or both twins are suspected of having an ASD (Autism, atypical autism or PDD).

To date, 20 MZ individuals(including 9 completed pairs) and 33 DZ individuals(including 8 completed pairs) aged twelve to fourteen, have been assessed using the ADI-R and ADOS. Different examiners completed the ADOS and ADI-R with each twin in order to minimize rater bias. In order to maintain quality and high levels of inter-rater agreement, examiners maintain reliability and coding disagreements are resolved by consensus.

Data were examined for diagnostic agreement by zygosity using both the Autism cut-off and an ASD threshold on the ADI and ADOS. ADI-R scores are divided into 4 domains. The threshold on this instrument for ASD was determined to be a score above published thresholds on three domains with a score that was +/-2 on the remaining domain.

Results:

Discrepancy between parent report and examiner observation was more marked for MZ than for DZ twins when using the Autism threshold on the ADOS and ADI.

The level of agreement between the ADOS and ADI when using the ASD cut-off for MZ twins was 80% and the rate for DZ twins was 85%. The level of agreement between the ADOS and the ADI when using the Autism cut off for MZ twins was 30% and the rate for DZ twins was 76%.

Conclusions:

This pattern of preliminary data suggests there are contrast effects in parent reporting that are more pronounced for MZ twins than DZ twins when using the Autism cut-off on the ADOS and ADI. It is much less likely that a parent will report concerns about an MZ twin when their co-twin has a diagnosis of an ASD even when autism –specific behaviors are observed by an examiner. If these findings are confirmed, they suggest possible rater bias and contrast effects. Such biases may have implications for twin and family studies of ASD.

120.27 27 A Twin Study of Gesture Execution, Imitation, and Identification. J. L. Stevenson*, N. A. Krause, E. K. Schweigert, H. H. Goldsmith and M. A. Gernsbacher, *University of Wisconsin-Madison*

Background: Persons on the autism spectrum tend to be less proficient than persons not on the autism spectrum at imitating gestures. Theorists have attributed less-proficient imitation to a myriad of interpersonal and intrapersonal deficits, such as a lack of a "sense of self" or a lack of a "subjective awareness of others" (Gallese, 2006; Harris, 2003; Rogers et al., 2003). However, empirical research documents that persons on the autism spectrum tend to be equivalently proficient at identifying other persons' gestures, including identifying the intentionality of other persons' gestures (Aldridge et al., 2000; Carpenter et al., 2001; Hamilton et al., 2007; Russell & Hill, 2001; Sebanz et al., 2005). Moreover, empirical research documents that persons on the autism spectrum are more proficient at imitating gestures than they are at executing gestures, without the guide of another person's demonstration (Alexander et al. 1992; Dewey et al., 2007; Hill, 1998; Mostofsky et al., 2006; Kees et al., 2006; Zoia et al., 2002). Thus, the source of their lower proficiency appears to reside in action execution, not social cognition.
Objectives: To investigate cotwins' proficiency and similarity in executing gestures (to an examiner's verbal request), imitating gestures (to an examiner's demonstration), and identifying gestures (to a video demonstration) using the well-established Praxis Test of the Boston Diagnostic Aphasia Exam.
Methods: Participants comprised 45 pairs of twins, age 4;2 to 20;3, who were recruited to the study because one or both cotwins of each pair met criteria for the autism spectrum on both the SCQ and the ADOS.
Results: Across all participants, proficiency in identifying, executing, and imitating gestures increased with age ($F(1,87)=28.27$, $p<0.001$; $F(1,75)=7.04$, $p<0.001$; $F(1,83)=12.54$, $p<0.001$, respectively). Similarly, across all participants, identifying gestures (M = 85%) was more proficient than imitating gestures (M = 61%), which was more proficient than executing gestures (M = 52%). Furthermore, participants who did versus did not meet criteria for the autism spectrum differed more dramatically in their proficiency in executing (44% vs. 70%) and imitating (53% vs. 78%) gestures than in their proficiency in identifying gestures (81% vs. 94%; $F(2,144)=5.02$, $p<0.01$, with participants' age as a covariate).
Finally, cotwins concordant for the autism spectrum were highly similar in their proficiency in executing gestures (intraclass R=.87, N=17), imitating gestures (R=.73, N=15), and identifying gestures (R=.76, N=12), whereas cotwins disconcordant for the autism spectrum were dissimilar (execution R=-.04, N=28; imitation R=-.02, N=26; identification R=-.13, N=26). Monozygotic cotwins concordant for the autism spectrum were highly similar in their proficiency in executing (R=.93, N=13), imitating (R=.93, N=11), and identifying gestures (R=.78, N=10), whereas monozygotic cotwins disconcordant for the autism spectrum were not all similar, despite their 100% genetic overlap (execution R=-.50, N=8; imitation R=-.42, N=7; identification R=-.33, N=8).
Conclusions: Performance on the Praxis Test distinguishes persons on the autism spectrum from those who are not. Moreover, praxis performance is highly similar for monozygotic cotwins who are concordant for the autism spectrum, suggesting that praxis performance taps systematic processes more specific than whatever processes contribute to meeting the diagnostic threshold.

120.28 28 Gender Effects in Autism Spectrum Disorders: Symptom and Intelligence Differences in a Population-Based Twin Study. K. Dworzynski*[1], F. Happé[2] and A. Ronald[3], (1)*Institute of Psychiatry, King's College London*, (2)*Institute of Psychiatry, KCL*, (3)*Birkbeck College, University of London*

Background: The fact that males show a much higher frequency than females of both Autism Spectrum Disorders (ASDs) and autistic traits is a well established fact. Some researchers hypothesise this gender difference to be x-chromosome linked whereas others highlight the

role of intrauterine testosterone level. It is possible that the current diagnostic criteria are slanted towards a male stereotype of ASD, and are less well-suited to recognising ASD in females.

Objectives: The aim of this study was to explore gender differences in ASD and ASD-like traits in a large population-based sample of twins. Because information on symptom/trait levels and intelligence are available independent of diagnosis, this sample allows investigation or possible biases in recognition as well as patterns of genuine male-female differences.

Methods: The Twins Early Development Study (TEDS) is a representative population-based UK twin study of all twins born in England and Wales in 1994-6, of which approximately 1% meet diagnostic criteria for autism, Asperger Syndrome or atypical autism. 12659 families provided data at first enrolment and have been contacted regularly since. 189 children of actively participating families met diagnostic criteria for ASD in 2007 according to parental interview with the Development and Wellbeing Assessment (DAWBA; Goodman et al., 2000). Data are available for IQ at ages, 2, 3, 4 and 7 years (with teacher assessments and national curriculum level at age 7), as well as autistic trait data (as assessed by the Childhood Autism Spectrum Test screening questionnaire, Scott et al., 2002) at age 8 (parental rating) and 12 years(parental and teacher rating). Gender differences in IQ and profiles of core symptoms domains (social / communication impairments and restricted, repetitive behaviours or interests) were analysed for diagnosed children and compared to non-diagnosed children with low or high ratings of ASD-like traits.

Results: Our findings suggested different patterns of gender effects in diagnosed versus high ASD-trait non-diagnosed samples. We found the expected disadvantage for IQ in females (versus males) with diagnosed ASD. However, in girls not diagnosed but with strikingly high ASD-like trait scores, no such IQ disadvantage was found. ASD-traits were more marked in boys than girls across the general population, but not in diagnosed cases or non-diagnosed cases with very high ASD-like traits.

Conclusions: The pattern confirmed previous findings that in the general population total autistic traits were more apparent in boys than girls, and that IQ is lower among diagnosed girls than diagnosed boys with ASD. However, the fact that non-diagnosed but high ASD-trait girls show no IQ disadvantage may suggest that probability of diagnosis is affected by IQ-level in girls more than in boys. In other words, ASDs, and especially more subtle forms of ASD, may be harder for clinicians to recognise in girls, especially in the presence of normal or high IQ.

120.29 29 Eye Color as a Potential Clinical Phenotype of ASD. C. J. Ferretti*[1], J. Pinto-Martin[2], M. C. Souders[2] and S. E. Levy[1], (1)*Children's Hospital of Philadelphia*, (2)*University of Pennsylvania*

Background:

Recent epidemiological studies have shown increased interest in eye color variation among medically relevant populations. Eye color has proven relevant to risk of macular degeneration, glaucoma, and melanoma; and is significant to the phenotype of multiple genetic disorders, including Waardenburg, Angelman and Prader-Willi Syndromes. However, little is known about eye color and Autism Spectrum Disorder (ASD). The gene for eye color, *Herc2,* is located on chromosome 15, an area of interest for ASD. Additionally, melanin, the pigment responsible for eye color, may have a role in the ascending reticular activation system regarding arousal and ASD. The purpose of this study is to explore the relationship between eye color and ASD, regarding its genetics and physiology, its relationship to the development of ASD and its use in defining a clinical phenotype for ASD.

A 1994 study conducted on individuals born between 1936 and 1951 calculated the rate of blue eye color in the United States for non-Hispanic Caucasians as 33.8%. Due to immigration and changes in culture, the proportion of blue eyed individuals in the United States is decreasing, and may be lower for this study's population of subjects.

Objectives:

To observe eye color in a population of children with ASD in relation to dysmorphic features, cognition and the core deficits of ASD (impaired social interaction and communication, and restricted and repetitive behaviors). Demographic variables, such as ethnicity and gender will also be examined.

Methods:

Child eye color was observed during clinic visits from the PA-SEED (Study to Explore Early Development) population, and photographic records were made. Characterization was made by a clinician, both in person and photographically, and was validated by a second clinician. Basic eye color choices were used, including blue, green, hazel, brown and black.

Results:

Of the current sample of 34 children, 23 scored positive on one of the gold standard ASD diagnostic instruments (ADI-R or ADOS). 16 of these children rated their ethnicities as non-Hispanic Caucasian. The distribution of eye color for these 16 children was as follows: 8 blue eyed, 2 green eyed and 6 brown eyed. The male to female ratio was 14:2. Other syndromes and developmental disorders were also present in this population. Additional subjects will be recruited, and their results added to the sample. A larger sample is needed to report eye color statistics in non-ASD research subjects. Correlations regarding dysmorphic features and results of cognitive instruments will be reported when a larger sample is collected.

Conclusions:

50% of the non-Hispanic Caucasian children who scored on the ADOS or ADI-R had blue eyes, while 12.5% had green eyes and 37.5% had brown eyes. The increased percentage of children with blue eyes in the selected study population, compared to the general population distribution, deserves further exploration. Further investigation into the genetics and physiology of melanin production, its role in the brain and iris, and the timeline of its development may allow the use of eye color as one component of a clinical phenotype for a subset of the ASD population.

120.30 30 Differences in Clinical Presentation of Trisomy 21 with and without Autism. C. A. Molloy*[1], D. S. Murray[1], A. Kinsman[2], H. Castillo[1], T. Mitchell[1], F. Hickey[1] and B. Patterson[1], (1)*Cincinnati Children's Hospital Medical Center*, (2)*Greenville Hospital System Children's Hospital*

Background: Autism occurs ten times more often in children with Down syndrome than in the general population, but diagnosing co-occurring autism in children with Down syndrome and severe intellectual disability is challenging.

Objectives: The objective of this case-control study was to identify characteristics differentiating children with trisomy 21 with and without autism and to determine the extent to which severe cognitive impairment affects measures of autism symptomatology.

Methods: Twenty children with trisomy 21 and autism (cases) were compared to children with trisomy 21 without autism (controls) matched on chronologic age, race and gender. Communication, cognitive and adaptive behavior skills were assessed with standardized instruments. Medical history was reviewed and medical records were examined for early head growth. Scores on the diagnostic algorithm of the Autism Diagnostic Interview – Revised (ADI-R) were compared after adjusting for cognitive ability as measured by the Stanford-Binet (5^{th} ed.) nonverbal change-sensitive score.

Results: Cases performed significantly more poorly on all assessments. Mean case-control differences for matched pairs were all significant at $p < 0.0001$ for receptive and expressive language skills, cognitive skills and adaptive skills. Seven cases had a history of seizures compared to 1 control ($p=0.01$). After adjusting for cognitive ability, the mean scores on the Reciprocal Social Interaction, Communication, and Restricted, Repetitive and Stereotyped Behaviors domains of the ADI-R diagnostic algorithm remained significantly higher in cases compared to controls ($p < 0.0001$). All participants had decreased head size consistent with Down syndrome, with no case-control differences.

Conclusions: Children with trisomy 21 and autism have significantly more impaired brain function than children with trisomy 21 without autism. However, the deficits in the core domains of social reciprocity and communication, and the restricted and repetitive interests are not entirely explained by the more severe cognitive impairment. This autism phenotype in children with trisomy 21 which includes an increased risk for seizures may indicate a widespread loss of functional connectivity in the brain.

120.31 31 The Role of FMR1 in Pragmatic Language Impairments Associated with Autism and the Broad Autism Phenotype. J. Klusek*[1] and M. Losh[2], (1)*University of North Carolina*, (2)*University of North Carolina at Chapel Hill*

Background: Strong evidence for the genetic basis of autism comes from twin and family

studies showing high heritability and the expression of subthreshold features among unaffected relatives that are believed to represent genetic liability for autism (i.e,. a broad autism phenotype, or BAP). Although a single "autism gene" has not yet been identified, approximately 6-15% of cases of autism can be traced back to a broader identifiable genetic condition. Fragile X syndrome (FXS) is one of the most common known causes of autism, with approximately 25-35% of individuals with FXS receiving a comorbid autism diagnosis. As all mothers of children with FXS are known carriers of the Fragile X Mental Retardation Gene (*FMR1)* gene in its premutation state, examination of this population allows for exploration of potential links between subtle autism symptomatology and known genetic etiology. Given that pragmatic language impairments are universally observed in autism, have been repeatedly documented in relatives of individuals with autism, and have been described as a principal feature of the BAP (Landa, Folstein & Isaac, 1991; Landa et al., 1992), such impairments are believed to constitute genetically meaningful component features related to autism. Examining pragmatic language skills in *FMR1* premutation carriers (i.e., mothers of individuals with FXS), may therefore help to illuminate a possible role of *FMR1* in the presentation of autism symptomatology and the broad autism phenotype.

Objectives: This study characterized pragmatic language abilities of mothers of individuals with fragile X syndrome (who are *FMR1* premutation carriers) in comparison to mothers of individuals with autism (who are at increased genetic liability to autism) and controls, in order to explore overlapping, potentially genetically-linked features of the broad autism phenotype, and to investigate the potential role of *FRM1* in the pragmatic language impairments associated with the BAP.

Methods: Semi-structured conversational interviews were conducted with mothers of individuals with FXS (n=10), autism (n=10), and typically developing children (n=10). Audio-visual recordings of the interviews were reviewed and the Modified-Pragmatic Rating Scale (M-PRS; Landa et al., 1992) was used to rate pragmatic language violations

Results: Mean pragmatic language impairment ratings of the FXS and autism mothers were significantly higher than those of control mothers; FXS vs. control, t=2.66, p=.028; autism vs. control t=4.64, p=.003. Mean ratings on the PRS were: 3.75 (SD=4.63) autism; 2.33 (SD=2.45) FXS; and 0.14 (SD=0.48) controls. Ratings of the FXS and autism mothers did not differ significantly (p>.29). Item analysis of M-PRS items showed tangential speech to be the most common pragmatic language error in both groups.

Conclusions: Both mothers of children with FXS and mothers of individuals with autism presented with overlapping impairments in pragmatic language skills, relative to controls. These findings suggest that *FMR1* could play a role in pragmatic language impairments described as part of the broad autism phenotype among relatives of individuals with autism.

120.32 32 Amygdala Function in a Known Genetic Cause of Autism.
E. Ballinger*[1], L. Cordeiro[2], J. Yuhas[1] and D. Hessl[2],
(1)*University of California, Davis*, (2)*M.I.N.D. Institute, University of California at Davis Medical Center*

Background: Amygdala dysfunction has been implicated in autism and is an excellent candidate for study because of its role in response to social stimuli and social behavior regulation. The amygdala has also been associated with several anxiety disorders. Anxiety is one of the most significant problems experienced by individuals with autism and is a core feature of fragile X syndrome (FXS), the most common known genetic cause of autism.
Objectives:

We investigated the relationships between the potentiated startle response, a biobehavioral probe of amygdala function, anxiety symptoms and autistic features in a specific cause of autism.

Methods:

We measured the startle response to auditory stimuli delivered during presentation of happy, fearful, and neutral faces and a non-social scrambled image. The difference in response magnitude between trial types was calculated. Anxiety symptoms were measured using the Anxiety, Depression and Mood Screen (ADAMS; Ebsensen et al., 2003), a parent report questionnaire. Severity of autistic symptoms was evaluated using the Autism Diagnostic Observation Schedule (ADOS; Lord, 2001).

The FXS group consisted of 24 individuals (15 boys and 9 girls) ranging in age from 5 to 25 years (mean: 15, SD: 6) and a mean IQ of 65 (SD:16). The idiopathic autism group contained 22 boys ranging in age from 12 to 22 years (mean: 17, SD: 3) with a mean IQ of 74 (SD: 23). The control group was 13 children (5 boys 8 girls) with typical development ranging in age from 4 to 17 years (mean: 11.5 SD: 4) and a mean IQ of 112 (SD: 14).

Results:

The FXS group was significantly less responsive than controls on all trial types other than happy faces, which approached significance. ADOS scores were positively correlated with responses to all trial types except happy faces. The FXS and autism groups both scored significantly higher on the ADAMS compared to controls but were not significantly different from each other. ADAMS scores were positively correlated with ADOS scores in the FXS group but not in the idiopathic autism group.

Conclusions:

The difference in potentiated startle response between the FXS group and the control group suggests abnormal amygdalar function in FXS. The relationships seen here between anxiety symptoms and severity of autistic symptoms may represent a phenotype specific to autism as caused by FXS. Data collection is continuing in the autism group.

120.33 33 A 2.2Mb 1q42.2 Microduplication Including DISC1 in 2 Brothers with Autism and Mild Mental Retardation. A. Crepel[1], J. Breckpot[1], J. P. Fryns[1], J. Steyaert[2], K. Devriendt[1] and H. Peeters*[1], (1)*Center for Human Genetics, University of Leuven*, (2)*UPC-K.U.Leuven*

Background: A growing number of copy number variations (CNV) are detected in individuals with neurodevelopmental disorders. However, the interpretation is not always straightforward. Traditionally, causality is assumed when the CNV is not observed in the normal population and/or when it occurs *de novo* or segregates with the disorder in the family. In addition, the presence of one or more genes in the CNV that can be linked to the pathogenesis of the phenotype may lend further support for causality.

Objectives: We describe the identification and delineation of a 2.2Mb microduplication in 1q42.2 in 2 brothers with autism and mild mental retardation and discuss the possible causal relation of this duplication to the autism phenotype.

Methods: The duplication was detected by Array-CGH with clones from the 1 Mb BAC/PAC clone set (Sanger Institute Hinxton, UK). The aberration was further delineated to 2.2Mb with a full-tiling BAC array containing the chromosome 1 clones. By means of quantitative real-time PCR (qPCR) the breakpoints of the duplication were mapped and segregation in the family was investigated. qPCR was used to screen 260 patients with autism for *DISC1* duplications.

Results: The 2.2Mb duplication was present in the proband, his affected brother and the apparently unaffected father and paternal grandmother. Since this duplication was not present in 1577 Belgian persons, it was considered as a rare variant. Within this region the most interesting gene with respect to autism is *DISC1* (disrupted-in-schizophrenia 1) since it is known to be involved in schizophrenia and has recently been associated to autism and bipolar disorder. A group of 260 patients with autism was studied for the occurrence of *DISC1* duplications. In this screen no additional duplications were found.

Conclusions: This study is a typical illustration of the difficult interpretation of causality of a rare variant in neuropsychiatric disease. We conclude that the *DISC1* duplication is a rare variant that probably confers susceptibility for autism in the current family.

120.34 34 FOXC1 Is Required for Normal Cerebellar Development and Is a Major Contributor to Chromosome 6p25.3 Dandy-Walker Malformation. K. A. Aldinger*, W. B. Dobyns and K. J. Millen, *University of Chicago*

Background: Cerebellar malformations (CbM) are common human structural birth defects of the brain that affect an estimated 1/5,000 births and typically cause mental retardation, developmental delay, motor and visual impairments, and have been observed in a subset of patients with autism spectrum disorder (ASD). Dandy-Walker malformation (DWM) is the most common CbM and is linked to at least four loci in humans. DWM gene identification remains a challenge due to its complex inheritance pattern and frequent confusion with other malformations of the cerebellum and posterior fossa. However, identifying the molecular basis for malformations

of the cerebellum and posterior fossa provides a method to clarify whether these abnormalities represent distinct entities or examples of phenotypes along a spectrum of the same molecular pathogenesis. Objectives: To classify CbM among patients with 6p25.3 copy number variants (CNVs), identify the major DWM-causative gene on chromosome 6p25.3, and test the hypothesis that molecularly defined CbM represent an ASD subgroup. Methods: CNV mapping and MRI evaluation were performed for patients with chromosome 6p25.3 CNVs to determine the minimal region of overlap on 6p25.3 associated with CbM. Mouse in situ hybridization (ISH) expression analyses and examination of mouse mutants was performed for the eight 6p25.3 DWM candidate genes. Extensive analysis of Foxc1 mutant mice was also performed. Results: Human CNV and mouse ISH expression analyses identified FOXC1 as the major DWM-causative gene on 6p25.3. In parallel, examination of Foxc1 mouse mutants revealed striking deficits in early cerebellar development, including an early expansion of roof plate and choroid plexus and premature loss of Math1 in cerebellar rhombic lip progenitors. Mice with a hypomorphic Foxc1 allele additionally displayed abnormalities in midline fusion, foliation, and Purkinje cell morphology consistent with a mouse DWM-like phenotype. The expression of Foxc1 in the cerebellum-adjacent mesenchyme regulates secretion of trophic factors required for cerebellar development and implicates skull developmental abnormalities as an integral component of DWM pathogenesis. Additional MRI analysis indicated that mutation of the human FOXC1 gene alone is sufficient to cause cerebellar abnormalities, but not the full DWM phenotype. Three DWM deletion 6p25.3 patients were also diagnosed with ASD and an additional deletion 6p25.3 ASD patients were reported in the literature without MRIs to evaluate for CbM. Conclusions: FOXC1 regulates cerebellar development in both humans and mice, but must interact with other 6p25.3 genes to cause the complete DWM phenotype. Together, these studies provide novel mechanistic insight into the pathogenesis of both DWM and ASD and highlight the importance of reciprocal diagnostic evaluation for patients with these disorders identified in the clinic.

120.35 35 Chromosomal Anomalies in a Portuguese "Idiopathic" Autism Sample. F. Duque*[1], J. Almeida[1], R. L. Abreu[1], E. Matoso[2], I. Carreira[2], A. Vicente[3] and G. Oliveira[1], (1)*Hospital Pediátrico de Coimbra*, (2)*Universidade de Coimbra*, (3)*Instituto Gulbenkian de Ciência/Instituto Nacional de Saúde Dr. Ricardo Jorge*

Background: Autism is a complex neurodevelopmental and a predominately genetic disorder defined by impaired reciprocal social interaction, communication and restricted, repetitive and stereotyped behavior. Approximately 2%-5% of individuals with autism spectrum disorder (ASD) have some form of chromosomal abnormality. The most common location is the chromosome 15q11-q13 region.

Objectives: This study aims to assess the chromosomal abnormalities found in a large sample of Portuguese children with idiopathic autism, observed over several years at our Unit.

Methods: Assessment of ASD entailed extensive interaction with patients in a clinical setting, the majority of who return frequently for follow up. ASD was diagnosed using ADI-R, CARS and DSM-IV-TR criteria. A comprehensive clinical history was collected, including the pre and per natal periods. We excluded the non-idiopathic ASD patients (Rett, Fragile X, neurocutaneous syndromes, endocrine, metabolic, trisomy 21 and other genetic disorders). High-resolution cytogenetic analyses were performed using peripheral blood lymphocyte cultures by standard protocols. Molecular cytogenetic was performed using paint and subtelomerics probes to clarified rearrangements.

Results: Of the 634 ASD patients with a male to female ratio of 4:1, 526 subjects were considered idiopathic (83%). They all had ADI-R positive and a 35 median CARS result. The median for Global Developmental Quotient (GDQ) was 62 and for Global Intellectual Quotient was 78. Within these group, nineteen subjects (3,6%), with ADOS positive and a 36 median CARS result (P_5 =30; P_{95}=52), presented chromosomal abnormalities. The median for GDQ was 44 and for Vineland Adaptive Behavior composite was 32 months (median chronological age=108 months). The chromosomal abnormalities were most frequently located on ch15q11-13 (FISH analysis) – 6 patients. Two siblings presented 46,XX del(5)(p15.2p15.2). The other chromosomal abnormalities were: two on 46,XY del(9)(pter); one each on 47,XY+r.ishr(15); 46,XYdel(1)(q); 46,XY rec(7)dup(7)ins(7)(q21.2p15.1p13)/mat; 46,XYdel(8)(p23.3); 46,XYdup(5)(pter); 46, XXinv(9)(q12q34.1); 46,XYinv(6)(q21q23.1); mos

47,XYY(26)/45,X(4); mos 46, XY,add(12)(p13.3)/46,XY.

Conclusions: Our findings corroborate other researches for overall prevalence of chromosomal abnormalities. Cytogenetic studies, that may guide molecular studies by pointing to relevant inherited or *de novo* chromosomal abnormalities, are a significant and worth doing initial approach for all idiopathic ASD. Finding chromosomal abnormalities may in fact provide a valuable contribution for genetic counseling of families and also to the identification of candidate gene regions for the disease.

120.36 36 Autism Genetic Database (AGD): a Comprehensive Database Including Autism Susceptibility Gene-CNVs Integrated with Known Noncoding RNAs and Fragile Sites. Z. Talebizadeh*[1], G. Matuszek[2] and R. Aldenderfer[1], (1)*Children's Mercy Hospital and University of Missouri-Kansas City*, (2)*University of Kansas*

Background: Autism belongs to a broad-spectrum of conditions known as autism spectrum disorders (ASD). To date, numerous susceptibility genes and genomic copy number variations (CNVs) have been reported in association with autism. However, in most cases the underlying causative genetic mechanisms are not fully understood. Recent developments in molecular genetic technologies and knowledge have introduced new avenues to be explored, in particular, for complex disorders. A good example is gene regulatory factors such as noncoding RNAs (ncRNAs) which are highly expressed in the nervous system. More recently, a study conducted by our group (Talebizadeh et al., 2008) and a report by Abu-Elneel et al. (2008) suggested that microRNAs, a group of ncRNAs, should be evaluated in the etiology of autism.

Objectives: In an effort to make all reported genomic features associated with ASD (i.e., susceptibility genes and CNVs) and their potential relationship with other genomic features impacting on human disease (e.g., ncRNAs and fragile sites) accessible to the scientific community, our research group designed the Autism Genetic Database, an open source database.

Methods: The Autism Genetic Database (AGD) system is installed on an Ubuntu Linux server and employs MySQL as a relational database management system (RDBMS) and Apache 2.0 as a web server platform. In AGD, data are searchable and displayed in either a genome browser or tabular format.

Results: Currently, a total of 145 and 473 autism susceptibility genes and CNVs respectively, plus 904 ncRNAs (i.e., microRNAs and snoRNAs) and 120 fragile sites (i.e., rare or common) grouped and organized by feature type are stored in AGD. This resource will be routinely updated and upgraded as new information relating to ASD becomes available. The existence of a comprehensive repository for the genomic information pertaining to ASD is crucial for the advancement of computational research into the field. The web interface provided by AGD will enable researchers, for example, to quickly identify specific ncRNAs within or close to reported autism candidate genes or CNVs in autistic subjects. Furthermore, the availability of such an integrated and comprehensive database will provide a valuable opportunity to explore and test autism genetic models.

Conclusions: While databases to maintain both autism susceptibility genes [AutDB (Basu et al., 2008)] and CNVs [Autism Chromosome Rearrangement Database (Marshall et al., 2008)] have been recently developed, the function of these available resources is to catalogue the relevant subset of autism related genomic data. While this information is useful to the research community, these currently available tools have a limited functionality with regards to the type of cross-talk search for which AGD has been designed.

120.37 37 Novel Copy Number Variation in Autism. S. Lund*[1], D. Pinto[2], E. L. Crawford[1], C. Marshall[3], S. Thomson[1], B. Yaspan[1], O. Veatch[1], S. W. Scherer[2] and J. Sutcliffe[1], (1)*Vanderbilt University*, (2)*The Hospital for Sick Children*, (3)*Hospital for Sick Children*

Background: Autism is a neurodevelopmental disorder that affects approximately 1 in 150 individuals and is characterized by deficits in reciprocal social interaction, communication and patterns of repetitive behaviors and restricted interests. Twin and family studies indicate high heritability, but evidence supports a highly complex architecture for the underlying genetic etiology. Recent discoveries point to Copy Number Variation (CNV) as an important class of rare variation that may cause or increase risk for autism. Objectives: The objectives of this study were to screen autism probands and parents for

evidence of CNV to identify loci that cause or confer susceptibility for autism. Methods: A series of 49 autism probands ascertained at Vanderbilt were screened on the Affymetrix 6.0 SNP platform. Raw genotype data was analyzed using multiple algorithms, including Partek, dChip, and AffyConsole, to maximize sensitivity and specificity of CNV detection. Variants predicted by two or more algorithms were prioritized for experimental validation. For a subset of probands, parents were genotyped on the Affymetric 6.0 arrays to determine whether predicted CNV was inherited or de novo. Parental samples were included in validation experiments, which primarily involved qPCR on the Roche LightCycler 480 using SybrGreen and/or Universal Probe Library (UPL) assays. Results: Analyses of the Affymetrix 6.0 data resulted in 3,265 CNV predictions in all, and of these 670 (20.5%) were called by two and 351 (10.7%) by three algorithms. Among CNV predictions, 1170 (36%) identified regions containing annotated genes. The majority were gains (1994, 61%), with only 39% predicted to be losses (1271). Only 670 (20.5%) and 351 (10.7%) CNVs were detected by two or three algorithms, respectively. Mean and median sizes for this group were 171kb and 73kb, respectively. Prioritized variants were validated using qPCR, and of those detected by two or more algorithms, all were confirmed and all found to be inherited. Validated CNVs identified loci previously implicated in mental retardation and/or point generally to neuronal cell surface molecules with a range of specific functions including cell adhesion, migration, synaptic vesicle release and cellular signaling. Conclusions: We have conducted a genome-wide SNP-based screen for CNV in a small cohort of autism probands, and as expected, have identified a number of inherited variants very likely to cause or contribute to risk in these families. The fact that most CNV in autism are inherited makes their interpretation more difficult. Possible explanations include reduced penetrance in the parents or that a greater overall mutation burden in probands who contain multiple CNVs. Lending support for specific CNVs is previously documented involvement of a gene in dominantly inherited MR or CNVs previously identified in autism in both de novo and inherited states. DOCK8 is an example of one that fits both of these scenarios. We would predict that several of the variants identified will point to genes that contain rare mutations in non-CNV-containing subjects. In conclusion, the findings reported here further underscore the important role that CNV plays in the genetic etiology of autism.

120.38 38 Microdeletions and Microduplications at 15q11.2 in Autism Spectrum Disorder in a Costa Rican Cohort. G. Cai*[1], L. Ospina[1], P. Jiménez[2], O. Bozdagi[1], J. G. Reichert[1], L. A. McInnes[1], T. Sakurai[1] and J. D. Buxbaum[1], (1)*Mount Sinai School of Medicine*, (2)*Hospital Nacional de Ninos*

Background: Recently, de novo copy number variants (CNVs) at 15q11.2 were reported to represent rare risk factors for schizophrenia in a large population-based study. An inherited deletion at the same locus was previously reported in a boy with neurological disorder, mental retardation and speech impairment. Furthermore, cases with Angelman syndrome due to the larger class I deletion, which includes the 15q11.2 region, are more likely to meet criteria for autism spectrum disorders (ASDs). The Central Valley of Costa Rica (CVCR) is a well-studied founder population that has been studied for neuropsychiatric disorders and ASDs.

Objectives: The broad goal of this study was to investigate the role of copy number variants (CNVs) in CVCR subjects with an ASD.

Methods: All ASD cases are being screened for CNVs using array-based comparative genomic hybridization (CGH) analysis and/or SNP arrays. QPCR and multiplex ligation-dependent probe amplification (MLPA) assays are being used to validate potential CNVs.

Results: We identified three subjects with ASDs in the CVCR that showed a CNV at 15q11.2. The CNV occurs between BP1 and BP2 (chr15:20089383-20630718, NCBI Build 35) in 15q, and includes four genes (*TUBGCP5*, *CYFIP1*, *NIPA2* and *NIPA1*). A CNV loss arose *do novo* in one case, while two CNV gains were inherited. All three subjects are male with an autism diagnosis. One case with a CNV gain has had reported convulsive episodes, and has macrocephaly and moderate cortio-subcortical atrophy, but EEG tests are normal in all cases. In the case with the *de novo* CNV loss, the mother had language delay (spoke late and had articulation problems). Functional analyses in mice indicate that haploinsufficiency of *CYFIP1* can result in abnormalities in synaptic plasticity.

Conclusions: CNVs at 15q11.2 were found in ASD in subjects from the CVCR. Functional studies support a role for one of these genes in synaptic plasticity. Our findings provide further support for a common pathogenic pathway in some cases of

schizophrenia and of ASDs. We are examining whether this results from pleiotropic effects of the implicated genes or from an intermediate phenotype that might increase risk for both ASD and schizophrenia.

120.40 40 A High Resolution CNV Survey of the GABA Gene Family and Additional Autism Candidate Genes. D. J. Hedges*[1], H. N. Cukier[1], D. Q. MA[1], J. M. Jaworski[1], P. L. Whitehead[1], H. H. Wright[2], R. K. Abramson[2], S. E. Echandia[3], Z. M. Kozhekbaeva[3], L. Nathanson[3], J. P. Hussman[4], J. Haines[5], M. L. Cuccaro[1], J. R. Gilbert[1] and M. A. Pericak-Vance[1], (1)*University of Miami Miller School of Medicine*, (2)*University of South Carolina School of Medicine*, (3)*University of Miami*, (4)*Hussman Foundation*, (5)*Vanderbilt University*

Background: Autism has a strong genetic component, but studies over the past decade have demonstrated that the underlying genetics are complex. Previous research suggests an important role for copy number variants (CNVs) in autism risk and indicates a strong association of CNVs with the autistic phenotype. Gamma-aminobutyric acidGABA) is the primary inhibitory neurotransmitter in the adult human brain. The chromosome 4 GABR cluster has previously been implicated in autistic disorder through both cytogenetic alterations as well as association with SNPs in the gene. Consequently, genes encoding for proteins involved in the GABA network represent excellent candidates for possible involvement in autism.

Objectives: While several studies have now conducted whole-genome surveys of structural variation in autistic individuals, we sought to achieve a significantly higher resolution analysis by employing a candidate gene strategy, primarily focused on GABA related genes. Using this approach, we have the ability to detect smaller scale structural variants that remain undetectable using standard whole genome CGH arrays.

Methods: Custom 1x244k Agilent comparative genomic hybridization (CGH) arrays were designed covering GABA related genes, as well as 28 additional autism candidate genes, including Neurexins 1-3 and Neuroligins 1-4, and SHANK3. Collectively, our probes spanned a total of 15 Mb with a density of approximately 1 probe every 150 nucleotides. 250 autism cases and 250 control individuals are currently being evaluated by aCGH. All experimental and control samples were hybridized vs. a single reference sample. Putative CNVs detected via aCGH will subsequently be validated using either standard PCR followed by gel electrophoresis or real-time quantitative PCR, depending upon the predicted size of the event.

Results: **Preliminary results indicate putative CNVs in two autism candidates.**

Conclusions: Pending validation of CNV events and additional analyses.

120.41 41 Feasibility for Detecting Epigenetic Abnormalities in Autism Brain. R. Person*, S. Kim, X. Zhang, Y. H. Jiang, R. Chen, Y. Li, W. Li and A. Beaudet, *Baylor College of Medicine*

Background: There is increasing evidence that *de novo* and recent mutations at any one of many heterogeneous loci cause a substantial fraction of autism. These findings are entirely consistent with the high heritability of autism, as evidenced by the high concordance between monozygotic (MZ) twins. Yet, the etiology of autism remains unknown for a large fraction of individuals, particularly for nondysmorphic, higher functioning males. Epigenetics refers to regulation of gene expression without change in the underlying DNA sequence. Important, analyzable components of epigenetic expression include expression of mRNA and miRNA, DNA methylation, and histone modifications. Epigenetics plays at least some role in the etiology of autism as evidenced by the fact that usually maternal but not paternal interstitial duplications of chromosome 15q11-q13 cause autism. Epigenetic abnormalities could be more widely important in the etiology of autism, and could contribute to the heritability seen in MZ twins if epimutatations arose prior to MZ twinning.

Objectives: To develop and implement methodologies to be used in finding epigenetic aberrations associated with or causing autism focusing on the use of postmortem brain. As a proof of principle, we wished to demonstrate the feasibility of using existing methods to detect the known epigenetic aberrations within 15q11-q13, responsible for Prader-Willi syndrome (PWS) and Angelman syndrome (AS) syndromes.

Methods: To investigate the presence or absence of DNA methylation, a combination of two methods was used. Methylated DNA immunoprecipitation (MEDIP), utilizing an antibody against methylated DNA, was used to detect the presence of methylated sites. An enzymatic method that utilized the restriction enzymes *Mcr*BC and *Hpa*II and subsequently amplification was used to detect unmethylated sites. Histone modifications were examined using

native chromatin immunoprecipitation (N-ChIP), followed by analysis either using Agilent microarrays or massively parallel Solexa DNA sequencing. Finally, the expression of 723 human and 76 human viral miRNAs were examined using the Agilent human miRNA (V2) microarray system.

Results: Using methodologies to examine the presence and absence of DNA methylation, we confirmed the ability to detect the known abnormalities in PWS and AS brain. Using NChIP to detect histone H3 lysine 4 trimethylation, a marker of active transcription, we confirmed its presence exclusively on the paternal *SNRPN* allele – present in AS but not PWS individuals. Finally, we found a significant upregulation of three miRNAs in 6 of 20 autism and in 0 of 20 control cerebellum samples.

Conclusions: We have demonstrated the ability to use these methodologies to detect known epigenetic abnormalities in PWS and AS brain and the feasibility of detecting changes in autism brain if they occur. We plan to apply all of these methodologies to compare autism and control brain tissue. Additionally, we have shown a significant elevation of three miRNAs in a subset of autism cerebellum samples.

ACKNOWLEDGMENTS: Simons Foundation SFARI, March of Dimes, William Stamps Farish Fund, NIH HD-037283, Autism Speaks, NAAR, AGRE, Harvard Brain Bank/Autism Tissue Project.

120.42 42 Global Methylation Profiling of Lymphoblastoid Cell Lines Reveals Epigenetic Contributions to Autism Spectrum Disorders.

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Background: Epigenetic mechanisms have been suggested as contributing factors in higher-order regulation of aberrant gene expression in autism spectrum disorders (ASD). One such mechanism, DNA methylation, involves the addition of a methyl group onto the C5 position of CpG dinucleotides. An increase of methylated CpG sites, particularly in the promoter region, is associated with transcriptional repression by either disruption of transcriptional machinery binding or recruitment of repressive methyl-binding proteins.

Objectives: The current study utilizes two complementary genomic approaches to globally identify genes regulated by methylation in lymphoblastoid cell lines (LCL) derived from monozygotic twins (MZ) discordant in diagnosis of autism and nonautistic sibling controls. The use of discordant twins and unaffected siblings enabled identification of epigenetic differences between genetically identical twins, as well as differences significant across all autistic individuals compared to nonautistic controls.

Methods: Two distinct forms of DNA microarray analyses were conducted on LCL from 3 pairs of discordant monozygotic twins and nonautistic sibling controls. Firstly, a methylated CpG island recovery assay (MIRA) was used to enrich the methylated fraction of genomic DNA. Enriched fractions were hybridized onto CpG island microarrays to identify genes with differentially methylated CpG island regions. Secondly, gene expression microarrays were utilized to identify methylation-sensitive genes exhibiting differential response between discordant MZ twins to treatment with a global methylation inhibitor, 5-Aza-2-deoxycytidine. Datasets from these analyses were analyzed using Ingenuity Pathway Analysis and Pathway Studio 5 software. The methylation status of candidate genes identified from both analyses was confirmed using bisulfite sequencing or methylation-specific PCR.

Results: Methylation profiling revealed many genes differentially methylated between discordant MZ twins and between twins and unaffected siblings. Bioinformatics analysis of the differentially methylated genes demonstrated enrichment for high level functions including gene transcription, inflammation, nervous system development, and cell death/survival. The overlap of genes identified in both analyses provided a stringent method of prioritizing ASD candidate genes. One hypermethylated candidate gene, BCL-2, was chosen for further study because of its anti-apoptotic functions, role in proper neurodevelopment, and reported protein decrease in autistic brain. Another gene, retinoic acid receptor (RAR)-related orphan receptor, RORA, also identified as hypermethylated in autistic individuals was chosen for its roles in Purkinje neuron differentiation, regulation of circadian rhythm, and protection against oxidative stress. In autistic individuals, there was a 2.5-fold and 2-fold decrease in gene expression for BCL-2 and RORA, respectively. Reactivation of gene expression was observed following treatment with

the methylation inhibitor, 5-Aza-2-deoxycytidine, as confirmed by qRT-PCR. An increase of methylated CpG residues within CpG island and promoter regions of BCL-2 and RORA was demonstrated by bisulfite sequencing and methylation-specific PCR in genomic DNA of LCL from autistic individuals.

Conclusions: Global methylation profiling of lymphoblastoid cell lines from autistic individuals highlight the role of epigenetic regulation in idiopathic autism and reveals potential cellular pathways through which this regulation may occur. In addition, a number of differentially methylated genes identified from these studies corroborate aberrant gene expression previously characterized in ASD.

This study was supported by Autism Speaks, Grant #2381.

120.43 43 Investigation of Post-Transcriptional Gene Regulatory Networks Associated with Autism Spectrum Disorders by MicroRNA Expression Profiling Using Lymphoblastoid Cell Lines. T. Sarachana*[1], R. Zhou[2], G. Chen[2], H. Manji[2] and V. W. Hu[1], (1)*The George Washington University Medical Center*, (2)*National Institutes of Health*

Background: Autism spectrum disorders (ASD) are neurodevelopmental disorders with a pattern of qualitative abnormalities in three behavioral areas: reciprocal social interactions, communication, and restricted interests and repetitive behaviors. Previous gene expression profiling of monozygotic twins discordant in diagnosis or severity of autism revealed differentially expressed, neurologically relevant genes, suggesting that epigenetic factors, such as DNA methylation or microRNA (miRNA), may be involved in ASD.

Objectives: The purpose of this study was to investigate the post-transcriptional gene regulatory networks by miRNA expression profiling of lymphoblastoid cell lines (LCLs) in order to better understand the role of miRNAs in the pathobiology of ASD.

Methods: Global miRNA expression profiling using LCLs derived from 5 autistic individuals and their monozygotic co-twins and/or their siblings were performed using high-throughput miRNA microarray analysis. The potential targets for each miRNA were predicted using miRBase software. An inverse relationship between the transcript levels of the potential target genes and that of the respective regulatory miRNAs in the same LCLs was used to identify miRNAs that could be responsible for the differential gene expression observed between discordant autistic twins and affected-unaffected sib pairs. Biological functions and pathways associated with the potential target genes were analyzed using Ingenuity Pathway Analyses and Pathway Studio 5 software.

Results: The majority of the significantly differentially expressed miRNAs were found to target genes highly involved in neurological functions and disorders. The potential targets, moreover, were also linked to gastrointestinal diseases, inflammatory diseases, and estrogen receptor signaling, including androgen and estrogen metabolism. Among the miRNAs found to be significantly differentially expressed in LCLs were some that were previously identified as brain-specific or brain-related. In addition, a number of the predicted potential target genes were also found to be significantly differentially expressed by cDNA microarray analyses. Novel network prediction analyses of the potential target genes whose transcript levels show an inverse relationship to that of the respective putative regulatory miRNAs reveal association with autism and other co-morbid disorders, e.g., muscular dystrophy and gastrointestinal diseases. Many biological functions implicated in autism, such as memory and synaptic plasticity, were also highlighted.

Conclusions: MiRNA expression profiling using LCLs reveals that post-transcriptional regulation of gene expression by miRNA may be a key factor contributing to the dysregulation of genes associated with neurological functions implicated in the pathophysiology of autism, such as synaptic transmission and plasticity. Moreover, finding brain-specific and brain-related miRNAs differentially expressed in LCLs also suggests the use of LCLs as a surrogate tissue to study miRNAs expression in ASD.

This study was supported by Autism Speaks, Grant #2381.

120.44 44 Cytokine Polymorphisms and Their Potential Role in Autism. M. C. Mott*, M. F. Casanova, G. R. Fernandez-Botran, L. Sears, C. R. Tillquist and F. A. Crespo, *University of Louisville*

Background: Cytokines are a diverse group of soluble regulatory proteins that play an essential role in the regulation of inflammatory responses

and are involved in the regulation of both innate and acquired immunity. Cytokines and their receptors are often encoded by highly polymorphic genes; and some of these polymorphisms are responsible for the observed inter-individual differences in cytokine production and likely impact the immune response. In the last 10 years, evidence has accumulated that increased levels of some pro-inflammatory cytokines are present in the peripheral blood mononuclear cells of children with autism spectrum disorders (ASD); fueling the hypothesis that an abnormal immune response could be another component of this multifactorial disorder. It may be useful to hypothesize that there are phenotypes of the immune system predisposed to stronger or weaker inflammatory immune responses, and these phenotypes can manifest from several different combinations of genotypes of different cytokine genes with variable expression. Since cytokines are able to cross the placenta the maternal immunogenetic make up may also be associated with fetal pathogenesis of autism. Objectives: The main objective of the current study is to characterize different single nucleotide polymorphisms (SNPs) in selected cytokine genes in autistic subjects and their mothers. Methods: DNA samples from two different sources were included in this study: a) ASD patients and their mothers (n=20) from Coriell Cell Repositories (http://ccr.coriell.org/autism/); b) ASD patients and their mothers (n=17) recruited at the Department of Pediatrics (University of Louisville). Cytokine genotypes were determined using a cytokine genotype kit (Invitrogen, Carlsbad, CA). A broad cytokine single nucleotide polymorphism panel was targeted: IL-1α, IL-1β, IL-1R, IL-1RA, IL-4, IL-4Rα, IFNγ, TGFβ1, TNFα, IL-2, IL-4, IL-6, IL-10, and IL-12. Results: Analyses revealed that frequencies of certain genotypes for specific cytokines document significant differences in the following groups: mothers vs. controls and autistics vs. controls, for IL-6, IL-12, IFNγ, and IL-4R. Significant differences were also detected between autistics vs. controls for IL-4 and IL-1RA specific genotypes. Conclusions: This study shows that some genotypes likely affecting the overall balance of pro- and anti-inflammatory components of the immune response may be more prevalent in autistic patients and their mothers. Furthermore, the assaying of cytokine genotypes may permit characterization of immune endophenotypes within the autistic spectrum.

120.45 45 Brain Derived Neurotrophic Factor (BDNF) in Serum of Children with PDDs and Their Parents. K. Francis*, A. Dougali, K. Sideri, K. Dimas and E. Lykouras, *Athens University*

Background: Brain Derived Neurotrophic Factor (BDNF) is a protein widely expressed in the developing brain which is known to regulate neuronal cell survival, differentiation, and plasticity. BDNF has been implicated in the study of Autism among other various disorders, such as Depression and Schizophrenia. Albeit some contradictory findings in various age groups, a BDNF excess theory has been put forward. **Objectives:** In the present on going study we intend to compare its concentration in the serum both of 50 children with PDDs aged 30-42 months, and their parents with that in normal controls. We are also following up these children to explore the correlation of BDNF concentration fluctuation with their adaptive functioning. **Methods:** Individuals are assigned case status if they have a clinical diagnosis of autism, atypical autism, Asperger syndrome, or PDD-NOS, meet ADI-R criteria for autism or fall one point below threshold on one of its behavioral domain and meet ADOS-G criteria at least for PDD. Subjects are selected if they are of normal intelligence by the use of Leiter-R and they had no history or signs of any birth complications, seizures or a known cause of Autism such as Fragile-X or Tuberous Sclerosis. Since BDNF concentrations are altered in the presence of atopy, an allergy history is completed, total IgE is measured and skin prick tests are carried out for 10 common allergens. Their adaptive functioning is measured by the Vineland Adaptive Behavior Scales. Parents are assessed for depression symptoms using the Beck Depression Inventory and for feautures of the Broader Autism Phenotype using the Broader Phenotype Autism Symptom Scale (BPASS). The presence of any chronic disorder, apart from Depression or the current use of medications represents an exclusion criterion. Controls are matched for age and sex children in preparation for an orthopedic surgery and age and sex matched adult blood taken from a blood bank, with a total IgE less than 120 kU/ml. Children are to be reassessed at 48, 60 and 72 months of age. Blood is taken from the cubital vein of the participating subjects between 9 and 10.30 a.m. to minimize effects of a possible circadian rhythm of BDNF concentrations. BDNF levels are measured using commercial enzyme-linked immunosorbent assays (ELISA). **Results:** Results

from the first wave of 17 children (mean age 35,8±4,1 months and Non-verbal IQ 106±24) and their families (but no controls) showed that: a) BDNF serum levels in probands was negatively correlated to the severity of Autism symptomatology, as this is expressed with ADOS Total Score (r = -0,733, p=0,025), b) BDNF serum level in parents had no statistical significant correlation neither with age nor with the presence of symptoms of the broader autism phenotype, as indicated by BPASS scores, and c) Parents that did had allergies had a statistical significant higher serum level of BDNF (1928,3±409 vs. 1463,1±666, p=0,028).
Conclusions: The findings of 40 families and controls, along with the first 15 follow-up of probands (age 48months) will be presented at IMFAR 2009 conference.

120.46 46 Association of Oxytocin Receptor Gene Variants with Social Phenotypes of Autism Spectrum Disorder. D. B. Campbell*, D. Datta, S. T. Jones, E. B. Lee, J. Sutcliffe and P. Levitt, *Vanderbilt University*

Background: Several lines of evidence indicate that oxytocin, signaling through its receptor (OXTR), is important in a wide range of social behaviors. In attempts to determine whether genetic variations in the oxytocin signaling system contribute to autism susceptibility, four recent reports have indicated association of common genetic polymorphisms in the *OXTR* gene with autism spectrum disorder (ASD) (Wu et al, 2005, Biol Psych; Jacob et al, 2007, Neurosci Letters; Lerer et al, 2007, Mol Psych; Yrigollen et al, 2008, Biol Psych). Each of these studies involved relatively small sample sizes (57 to 195 families) and, where it has been examined, failed to identify association of *OXTR* polymorphisms with ASD and measures of social behavior in individuals with ASD.
Objectives: To attempt to replicate association of common polymorphisms in the *OXTR* gene with ASD in a larger sample, and to examine association of genetic variants in *OXTR* with phenotype scores of the ADI-R, ADOS, and SRS.

Methods: The sample consisted of 664 families with at least one offspring with a diagnosed ASD. Additional phenotype information was available for a subset of 334 families from the Autism Genetics Resource Exchange (AGRE) Consortium. Genotypes were determined at 9 markers in the *OXTR* gene by ABI Taqman assays. Family Based Association Test (FBAT) analysis was performed on ASD diagnosis as well as phenotype scores of the ADI-R, ADOS, and SRS.
Results: The *OXTR* 3′ UTR marker rs1042778 G allele was associated with ASD diagnosis (P=0.018), replicating precisely a previous report of significant association (Lerer et al, 2007). In contrast to previous reports, association of the rs1042778 G allele was also observed for the ADI-R social total domain (P=0.019) and for each of 4 social sub-domains (P<0.05) in the 334-family AGRE sample. However, the rs1042778 G allele was not significantly associated with ADI-R total scores of communication (P=0.076) and behavior (P=0.067). No other marker was associated with ASD diagnosis in the entire 664-family sample. The intron 3 marker rs2268493 T allele, although not significant for association with ASD (P=0.073), was associated with the autism cut-off on the ADI-R (P=0.046). Like the rs1042778 G allele, the rs2268493 T allele was associated with the ADI-R social total score (P=0.014) and 3 of 4 social sub-domain scores (P<0.05), but was not associated with ADI-R total scores for the communication and behavior domains. No *OXTR* marker was associated with phenotype scores on the SRS, and no consistent pattern was observed for any phenotype scores on the ADOS modules.

Conclusions: These results replicate the association of *OXTR* variants with ASD in a large study sample and suggest association of *OXTR* genetic polymorphisms with social aspects of ASD. These results should be interpreted with extreme caution because none of the nominally significant associations would survive an appropriate correction for multiple comparisons. However, the precise replication of previous results in an independent cohort and the biological plausibility of participation of the oxytocin signaling system in ASD suggest that functional polymorphisms of *OXTR* may contribute to ASD risk in a subset of families.

120.47 47 Examination of the AVPR1a Microsatellites in Relation to Human Promoter Activity. K. Tansey*, M. J. Hill, L. E. Cochrane, R. J. Anney, M. Gill and L. Gallagher, *Trinity College Dublin*

Background: Autism is a neurodevelopmental disorder encompassing three core areas of behaviour: deficits in communication, deficits in social behaviours and the presence of restricted repetitive behaviours. The neuropeptide vasopressin has been implicated in the aetiology of autism. It has been shown through animal models to mediate social cognition, encompassing

social memory formation, social recognition, and social motivation. These processes are impaired in autism. Through work in voles, a single functional microsatellite upstream from the arginine vasopressin receptor 1A (AVPR1a) was found to be associated with social behaviours (Hammock and Young 2001). In humans, three microsatellites are located in this region.

Objectives: We examined the effect of human microsatellite RS1 on the expression of AVPR1a using a reporter assay system.

Methods: Alleles were chosen based upon length of polymorphism repeat using a short and long repeat for each. Inserts contained the microsatellite repeat and the promoter region up to the start of transcription. Inserts for each length were cloned into the pGL3 basic vector (Promega, UK). Each construct was then tested in 2 different cell lines – CHO K1, and SH SY-5Y. Differences in the promoter activity between the different length repeats was then determined using a luciferase reporter assay system (Promega, UK).

Results: In both cell lines (CHO K1 and SH SY-5Y) no increases in relative expression levels compared to background were observed.

Conclusions: It is possible the microsatellite RS1 is inhibiting the promoter activity and further work will be performed to investigate this.

120.48 48 Association Study of Neurexin 1 and Neuroligin 3 & 4 Genes with French Autistic Patients. F. Laaghouiti[1], P. Gorwood[1], B. Golse[2], L. Robel[2] and N. Ramoz*[1], (1)*INSERM*, (2)*AP-HP*

Background: Beta-neurexin and neuroligin molecules form an intercellular adhesion complex sufficient to trigger formation of functional presynaptic elements. Mutations and copy number variants have been identified in neurexin 1 (*NRXN1*) and neuroligins 3 & 4 (*NLGN3 & NLGN4*) genes in autistic patients.

Objectives: Our goal is to identify association between autism and polymorphisms of *NRXN1, NLGN3* and *NLGN4* genes.

Methods: We performed a case-control study by genotyping 9 single nucleotide polymorphisms (SNPs) within *NRXN1*, *NLGN3* and *NLGN4* genes, using TaqMan® SNP Genotyping Assays, on 84 French autistic patients, 26 parents, and 143 healthy controls matching for the geographic origin. Distributions of alleles and genotypes were compared between patients and controls. Transmission disequilibrium test was carried out in families.

Results: SNPs were on Hardy-Weinberg equilibrium. No significant differences of frequency for alleles or genotypes were found between autistic patients and controls. In particular, no variation was observed for the missense mutation R451C in the *NLGN3* gene. No excess of transmission was showed from parents to patients.

Conclusions: No association between polymorphisms in *NRXN1*, *NLGN3* and *NLGN4* genes was identified with autism in this study.

120.49 49 Mutant Forms of PTEN Associated with Autism. R. E. Redfern[1], M. C. Daou[2], A. Gericke[1] and A. H. Ross*[2], (1)*Kent State University*, (2)*University of Massachusetts Medical School*

Background: The phosphatase and tensin homolog deleted on chromosome 10 (PTEN) was implicated for a subset of autistic patients with macrocephaly. Six independent studies have identified patients in this subclass that have one normal and one mutated PTEN gene. Because loss of both PTEN genes is embryonic lethal, we do not anticipate any patients with both PTEN genes mutated. The PTEN protein is a phosphatidylinositol phosphate phosphatase specific for the 3-position of the inositol ring. PTEN and phosphoinositide 3-kinase have opposing effects on PI(3,4,5)P3 and, consequently, on cell proliferation and survival. PTEN's structure consists of a short N-terminal PI(4,5)P2 –binding domain, a phosphatase domain rich in alpha-helix, a C2 domain dominated by beta-sheet and a C-terminal tail with several phosphorylation sites. Recently, we and others have proposed a model for regulation of PTEN by PI(4,5)P2. Efficient action of PTEN requires three steps. First, PTEN binds to PI(4,5)P2 in the membrane. Second, PTEN undergoes a conformational change that increases alpha-helical content and activates the phosphatase domain. Third, PTEN diffuses on the surface of the membrane and hydrolyzes PI(3,4,5)P3. Objectives: The autism-associated PTEN mutations might have a number of different effects, including null mutations with complete loss of PTEN phosphatase activity hypomorph mutations with reduced activity and gain of

function in which the mutation results in a novel function. A first step in determining the effects of these mutations is to express the mutated PTEN proteins and determine if they are active as a lipid phosphatase. Methods: Recombinant PTEN was expressed in bacteria. Binding of PTEN protein to lipid vesicles was measured by doping the vesicles with a dansyl-lipid. Fluorescence from the PTEN tryptophans is quenched by dansyl. As a result, the fluorescence from vesicle-bound PTEN is quenched. PTEN protein is titrated with the dansyl-doped vesicles, allowing calculation of binding constants. Conformational changes of PTEN were detected by infrared spectroscopy. The spectra shift depending on the content of alpha helix and beta sheet. Phosphatase activity was measured by a colorimetric assay in which free phosphate results in a green color. Results: The laboratories that discovered the autism-associated PTEN mutations did not characterize the resulting PTEN proteins. In this study, we characterized the histidine 93 to arginine (H93R) mutation, which is near the phosphatase active site. We found that the H93R mutation affects multiple steps of PTEN action. First, the mutation affects binding of PTEN to membranes bearing negatively charged lipids. Binding of H93R PTEN to phosphatidylserine-bearing membranes was more avid than that of wild type PTEN. Second, the phosphatase activity was decreased for H93R PTEN. Third, H93R PTEN showed increased localization in the nuclei of U87MG glioblastoma cells. Conclusions: The autism-associated H93R mutation of PTEN reduces but does not eliminate phosphatase activity. Furthermore, the mutation increases localization of PTEN in the nucleus. Further studies are needed to determine the consesquences of this increased nuclear localization.

120.50 50 PRKCB1 Gene Variants Influence Stereotypic Behaviors in Autism-Spectrum Disorders. R. Sacco[1], F. Rousseau[2], J. Hager[2], P. Curatolo[3], B. Manzi[3], R. Militerni[4], C. Bravaccio[5], C. Lenti[6], M. Saccani[6], S. Puglisi-Allegra[3], T. Pascucci[3], K. L. Reichelt[7] and A. M. Persico*[1], (1)*Univ. Campus Bio-Medico*, (2)*IntegraGen*, (3)*Univ. of Rome* , (4)*II Univ. of Naples*, (5)*Univ.* , (6)*Univ. of Milan*, (7)*Rikshospitalet/Univ. of Oslo*

Background: Autism is a complex neurodevelopmental disorder, likely encompassing multiple pathogenetic components. Single genes most likely influence a single component, rather than the entire set of autistic signs and symptoms. We have recently shown in 245 ASD patients that at least four principal components provide major contributions to autism pathogenesis, namely (I) a disruption of the circadian cycle associated with behavioral and sensory abnormalities, (II) dysreactive immune processes underlying both prenatal obstetric complications and postnatal excessive body growth rates, (III) a generalized developmental delay linked in some way to a "leaky kidney", and (IV) an abnormal serotoninergic modulation of neural circuits underlying stereotypies and mirror neuron-mediated social behaviors. PRKCB1 contributions to these components were assessed here.

Objectives: The purpose of this study is to assess whether the PRKCB1 gene variant associated with autism provides broad contributions to the pathogenesis of the disease or instead contributes to a specific component.

Methods: Marker variables from these 4 principal components were correlated with PRKCB1 genotypes at SNP rs3785392, previously found most associated with autistic disorder (Lintas et al, Mol Psychiatry E-pub March 4, 2008), in 201 ASD patients.

Results: The G allele at rs3785392 is significantly associated with the marker variable for component IV, verbal and vocal stereotypies (chi squared = 7.16, 2 df, $P<0.05$). Also motor stereotypies, another variable in component IV, display a non-significant trend in the same direction (chi squared = 4.53, 2 df, $P=0.1$). There is no association between rs3785392 and marker variables for components IA (sleep disorders), IB (hyperactivity), II (history of allergies) and III (level of verbal language development).

Conclusions: PRKCB1 gene variants associated with autism influence the disease phenotype in the area of component IV, especially in reference to stereotypic behaviors.

120.51 51 A Case-Control Association Study of Tic/Stereotypic Movement Phenotypes in a Missouri Twin Sample and Polymorphisms in the Dopaminergic and Nicotinic Acetylcholine Receptor Genes. L. Albores-Gallo*, A. Reiersen and R. Neuman, *Washington University at St. Louis Missouri*

Background: Tics and stereotypic movement disorders (SM) are defined in DSM-IV-TR (American Psychiatric Association, 2000) as clearly separate disorders, sometimes difficult to distinguish. SM represent a continuum of behavior present with the typically developing child population at one end of the spectrum, and extending into autistic disorder and other

pervasive developmental disorders (PDDs) at the other end of the spectrum. SM have similar co-morbidity patterns and family history as tics. These similarities between both disorders suggest that they may share the frontal-striatal abnormalities described for Attention-Deficit/Hyperactivity Disorder (ADHD), obsessive compulsive disorder (OCD), and tic disorders, and the genes implicated in these pathways**.**

Objectives: To investigate the association between a Tic Narrow Phenotype (TNP) & Tic/Stereotypic-Movements-Broad-Phenotype (TSMBP) and the following candidate genes: Dopamine transporter (SLC6A3, also referred to as DAT1), D4 receptor (DRD4) and the Nicotinic acetylcholine receptor CHRNA4 gene.

Methods: Participants from the population-based Missouri Twin Study sample (MOTWIN) were selected.
Measures: Parents and twins completed the **M**issouri **A**ssessment of **G**enetics **I**nterview for **C**hildren (MAGIC) (Todd et al, 2003) that queries present and past existence of all DSM-IV symptoms of psychopathology. Interviewers had college degrees (psychology or related background) and received a 6-week training course for the MAGIC interview. For this study we used the DSM-IV Tic disorder diagnoses, (transient, chronic, motor and vocal), Tourette syndrome (TS), Stereotypic movements, ADHD, OCD, and related diagnoses. Child Behavior Checklist CBCL/4-18 (Achenbach, 1991) was also completed by the parents. Of 1635 total subjects, 67 were assigned to the TNP which included DSM-IV transient (motor or vocal), chronic (motor or vocal), or Tourette Syndrome from the MAGIC-Parent interview; and 511 twins met criteria for TSMBP which included TNP+SM from MAGIC-Parent interview + 2 CBCL items (Nervous movements and Picks skin rated as 1 or 2). The average age of both phenotypes did not differ (approximately 13 ± 3.2 years).

Results: Cases with TNP and TSMBP had significantly higher co-morbidity for ADHD, OCD, Depression, conduct disorder and oppositional defiant disorder than controls ($p<.0001$ for each comparison). We found a significant association with rs6090384, a SNP (single nucleotide polymorphism) in exon 2 of the CHRNA4 gene on chromosome 20 (odds ratio 5.6, 95% CI=1.4-22.6) and TSMBP. No additional associations were found between DAT1 or DRD4 for TSMBP; nor were there any genetic associations found with TNP.

Conclusions: These results provide support for a putative role of a CHRNA4 variant in TSMBP. Replication studies are necessary to confirm these findings.

120.52 52 Whole Genome Association Studies in Autistic Spectrum Disorders Revisited: a Support Vector Machine Approach. P. Johnston*[1], D. R. Hardoon[2], C. Ecker[1], T. K. Clarke[1], E. Daly[3], J. Powell[4], D. Murphy[1] and M. R. C. AIMS Consortium[4], (1)*King's College London, Institute of Psychiatry*, (2)*University College London*, (3)*Institute of Psychiatry, King's College London*, (4)*Institute of Psychiatry*

Background: Autistic spectrum disorders (ASDs) are moderately common, highly heritable neurodevelopmental conditions with a strong genetic basis. Several lines of evidence support genetic factors as a predominant cause of ASDs. However, investigations' using conventional genetic approaches has been slow. To date no single biological or clinical markers have yet been identified. Recent years has seen an increase use of whole genome association studies (WGAS), specifically through the establishment of collaborative efforts such as Autism Genetic Resource Exchange (AGRE) and the Autism Genome Project. Still very little light has been shed on the complex aetiology of this polygenic disorder. Support vector machines (SVM), one method of machine learning, has the ability to classify data using a mathematical function which best discriminates two groups - also highlighting the most influential discriminatory factors. However nobody has yet applied a SVM approach on WGAS.
Objectives: To analysis whole genome association data using a SVM application, classifying individuals into ASD affected or unaffected groups. This data will be used to indicate which SNPs are the most influential in terms of the classification. This is the first known study to use a SVM approach on whole genome data.
Methods: A WGAS (Affymetrix 5.0) was conducted on 2879 individuals generated at the Broad Institute and data was kindly provided to the Autism Genetics Resource Exchange. The sample was comprised of 1385 affected and 1494 unaffected individuals, each with 390671 features (SNPs). A SVM analysis, using a linear kernel, was applied to the data using a leave-one-out

procedure.
Results: SVM achieved an overall classification accuracy of 74% of the total sample. When broken down into affected and unaffected results of 54% and 94% respectively where achieved. 10 SNPs where identified as having a high weighted effect in discriminating the ASD affected from the unaffected groups. These 10 SNPs included 2 on chromosome 2 (q37.2) within the CENTG2 gene region.
Conclusion: This is the first study examining whole genome data using a SVM approach. Even though only 54% of the affected individuals where correctly classified, this analysis approach did identify SNPs within a gene found previously to be associated with ASD. This highlights the potential valuable use of SVM analysis on whole genome association data.
Acknowledgments: Data was generated at the Broad Institute and provided to AGRE by Dr Mark Daly and the Autism Consortium.

120.53 53 Family-Based Association Study of the X Chromosome Reveals ASD Genes. E. R. Martin*[1], R. H. Chung[1], D. Q. MA[1], J. M. Jaworski[1], J. R. Gilbert[1], D. J. Hedges[1], J. Hoffman[1], A. N. Andersen[1], I. Konidari[1], R. K. Abramson[2], H. H. Wright[2], J. Haines[3], M. L. Cuccaro[1] and M. A. Pericak-Vance[1], (1)*University of Miami Miller School of Medicine*, (2)*University of South Carolina School of Medicine*, (3)*Vanderbilt University*

Background: The autism spectrum disorders (ASD) are a group of a complex neurodevelopmental disorders with a strong genetic component. The skewed prevalence toward males compared to females and evidence of linkage to the X chromosome in some studies suggests the presence of X-linked susceptibility genes for ASD.

Objectives: To identify X-linked genes in ASD using genome wide association data (GWAS) and a family based association test.

Methods: We have conducted the first analysis of GWAS data on the X chromosome in ASD families. We analyzed 1497 samples from 488 nuclear families from the MIHG Collaborative Autism Project (CAP), genotyped using the Illumina Human 1M beadchip, and a second independent dataset of 3304 samples from 630 ASD families from the Autism Genetic Resource Exchange (AGRE) 550K SNP dataset. Markers were analyzed using the XAPL, a family-based test of association, in each dataset separately and jointly in the combined data.

Results: Thirteen regions containing 28 genes were significant ($p<0.005$) in both datasets. Joint analysis of the combined datasets gave 15 significant ($p<0.001$) regions containing 15 genes. Taken together, the results most strongly implicate two genes, dystrophin (DMD) and patched domain containing 1 (PTCHD1). These genes replicate consistently in our two family datasets ($p<0.005$) and are significant in the combined analysis ($p<0.001$). Eight other genes were also significant in the datasets separately and in the joint analysis.

Conclusions: Family-based association analysis on the X chromosome has not been routine. It requires proper analytic tools and careful interpretation. Our results in two independent datasets provide strong support for involvement of DMD and PTCHD1 in ASD and suggest several other X-chromosome candidates.

120.54 54 Molecular Investigation of An Autism Risk Association Region on Chromosome 5p14.1. A. J. Griswold*[1], H. N. Cukier[2], P. L. Whitehead[2], I. Konidari[2], W. Hulme[1], D. Q. MA[2], J. M. Jaworski[2], D. Salyakina[1], L. Wang[1], D. J. Hedges[2], J. Haines[3], J. R. Gilbert[2] and M. A. Pericak-Vance[2], (1)*Miami Institute for Human Genomics*, (2)*University of Miami Miller School of Medicine*, (3)*Vanderbilt University*

Background: Autism is a highly heritable neuropsychiatric disorder. To date, however, no single causative gene has been identified through linkage or association studies, suggesting a complex genetic etiology. We have recently identified and validated a significant association in a novel region on chromosome 5 p14.1 (see Ma et al., this meeting). Though this region lacks any known genes or regulatory sequences, the clustering of association signals suggests that one or more nearby functional variants is responsible for the association.

Objectives: To use molecular techniques to examine the candidate region and determine the genetic variant on chromosome 5p14.1 responsible for the association peak.

Methods: We used a three pronged molecular approach to examine the candidate region. First, evolutionarily conserved regions in the peak area of association, as well as the exons of the nearest genes, CDH9 and CDH10, were sequenced in 100 autism cases and 100 controls. Secondly, CGH arrays were used to detect copy number variations (CNVs) located within the peak region and CDH9 and CDH10. Finally, a combination of

RT and RACE PCR was used to evaluate the expression of unannotated ESTs in the peak region and search for previously unidentified exons at the 5' end of CDH10 and 3' end of CDH9 that would extend them nearer to the association peak.

Results: Sequence analysis of 100 cases and 100 controls has identified variation at 50 known SNPs and 37 novel variants within the conserved regions near the association peak, 9 known and 26 novel variants in CDH10, including 2 nonsynonymous amino acid changes, and 12 known and 9 novel variants in CDH9, including 5 nonsynonymous amino acid changes. Novel CNVs were detected in a single autistic individual and arrays of higher density of coverage in this area are currently in process. RT-PCR suggested the expression of predicted ESTs near the association region in brain tissue. Finally, RACE PCR indicated a 150bp extension of the 5'UTR of CDH10, though not a novel exon.

Conclusions: Our preliminary results suggest that several molecular factors in the autism association peak region on chromosome 5p14.1 may contribute to the association signal. Novel sequence variations and CNVs are currently being validated in a larger dataset to assess their frequency in cases vs. controls. Moreover, analysis of the predicted ESTs and new 5'UTR extension of CDH10 may reveal variations which confer increased risk of autism.

120.55 55 Deficiency of Engrailed 2 (En2), the Autism Spectrum Disorder (ASD) Associated Gene, Produces Abnormal Development of Forebrain-Projecting, Monoamine Neurotransmitters Systems. L. Lin*[1], P. Sonsalla[1], S. Kamdar[2], J. H. Millonig[2] and E. DiCicco-Bloom[1], (1)*Robert Wood Johnson Medical School*, (2)*UMDNJ-Robert Wood Johnson Medical School*

Background:

We have found that *EN2* is associated with ASD in 3 datasets, and 4 other groups report associations in datasets of different ethnicities that exhibit allelic differences, observations that support *EN2* as an ASD susceptibility gene. We are using the *En2* mutant mouse (knock out, KO) as a genetically valid model to define the roles of *En2* during development. Significantly, *En2* is expressed prenatally in mid- and hindbrain regions where monoamine-containing neurons that project to the forebrain originate. In ASD, abnormalities in monoamines, especially serotonin (5HT), are well known and include increased blood levels in 1/3 of patients, altered rates of 5HT synthesis detected by PET scanning, and serotonin transporter gene (5-HTT) linkage. Furthermore, forebrain-projecting monoamine neurons play major roles in behaviors altered in ASD, including attention, mood, repetitive movements and self-injury. The therapeutic efficacy of monoamine modulating drugs provides additional evidence of altered monoamine function in ASD. A possible link between *EN2* and development of monoamine neurotransmitter systems prompted us to examine development of the major monoamine transmitters, norepinephrine (NE), dopamine (DA), 5HT and their metabolites, in *En2* KO and wild type (WT) mice.

Objectives:

Identify the role of *En2* in monoamine neurotransmitter system development using *En2* KO mutant as animal model.

Methods:

Cerebral cortex, striatum, hippocampus, amygdala, cerebellum, midbrain and pons/medulla were dissected from postnatal day 0 (P0), P7, P14, P21 and P60 WT and *En2* KO mice. Neurotransmitter levels were assessed by HPLC and tyrosine hydroxylase (TH) protein levels were assayed by Western blotting.

Results:

Overall, during development, monoamine transmitters were increased in mid/hindbrain regions but decreased in forebrain structures of *En2* KO mice. The greatest changes were in NE, with levels elevated 40-70% in cerebellum but reduced 30-60% in hippocampus from P7 to P21. Most forebrain regions displayed decreased NE levels at P14 and P21, while all mid/hindbrain regions showed increases. Reduction of NE levels in forebrain started as early as P0. However, by adulthood, P60, NE deficits were diminished, with 16% and 23% reductions in amygdala and hippocampus respectively, without changes in other regions, suggesting partial recovery as development proceeded. One potential mechanism, a deficit in NE synthesizing enzyme, TH, was supported by Western blot, which demonstrated a parallel 50% reduction in protein levels at P21 in KO hippocampus. 5HT and DA

exhibited smaller changes in brain regions at several ages, with similar mid/hindbrain increases and forebrain decreases, suggesting an overall regional delay/deficit in monoamine neurogenesis and/or axonal process elaboration. In contrast, there was no difference in regional GABA content.

Conclusions:

Development of forebrain-projecting monoamine neurotransmitter systems is disturbed by deletion of *En2*, producing elevated levels in mid/hindbrain regions and reduced levels in forebrain structures. These forebrain deficits partially recover as development proceeds. These observations provide one mechanism by which patterning gene abnormalities in the hindbrain can secondarily affect forebrain development, especially given known effects of monoamines on proliferation, survival and differentiation. We plan to further characterize brain region structure and function to identify the roles of *En2* during development.

120.56 56 Ancestry and Association Analysis of the AGRE Autism Families. B. Yaspan*, J. Haines and J. Sutcliffe, *Vanderbilt University*

Background: Autism is a common neurodevelopmental disorder characterized by deficits in language, reciprocal social interaction and patterns of rigid compulsive behaviors. Twin and family studies indicate that autism has a predominantly genetic etiology, and the presence of broader autism phenotype features in first degree relatives further supports heritability within families. While much progress has been made in recently in identifying rare variants associated with autism, progress in identifying and validating common allele effects has been more difficult due to what are presumed to be small effect sizes for a genetically heterogeneous disorder. Recent advances include development of dense genome-wide SNP datasets for analysis of association and copy number variation; one such dataset is derived from the AGRE family collection genotyped on the Illumina 550k SNP platform. Objectives: The objectives of this study were first to conduct a detailed analysis of ancestry, and secondly to utilize a staged design to assess allelic association in the AGRE 550k Illumina genotype data. Methods: In order to characterize ancestry in the AGRE families, we selected a subset of 5,000 SNPs from the Illumina 550k panel to infer ancestry of founders (parents) using STRUCTURE with samples from the eleven HapMap 3 populations as positive controls. Association was assessed by randomly splitting the AGRE families into training and test sets of equal size, and stratified by ancestry using the STRUCTURE results. Association was assessed by TDT on training set Caucasians and all SNPs with $p<0.001$ were examined in the test set for replication purposes. Results: Ancestry was determined for 1,228 out of 1,233 parental samples, including 95 individuals whose self-reported ancestry was unknown. Using TDT to test for association in families of European ancestry, we found 863 SNPs with a $p<0.001$ in the training set. Of these, 54 were also significant in test set Caucasians at $p<0.05$. By limiting the findings to those SNPs in which the direction of association was the same, 22 SNPs remained. One of these SNPs, rs13112011 located at 4p15.2, remained statistically significant after a conservative Bonferroni correction ($p = 3.94E-5$; OR 0.37, CI: 0.25-0.53). The SNP was also associated in families of Latino ancestry, but not in the African American or Asian families in the combined dataset. Statistical association among Caucasians was confirmed using FBAT and significance was attained in both a broad "Spectrum" ASD sample as well as narrowly defined "strict" autism families. Furthermore, several other SNPs around this SNP both up- and downstream were statistically significant as well. Haplotype analysis showed that rs13112011 specifically tags one haplotype that is significantly associated. This marker is located in an intergenic region between two spliced transcripts that have not been annotated. Conclusions: Using a two stage design, we have analyzed the publicly-available AGRE 550k data and identified markers that are associated in both an initial and follow-up replication subsample. While multiple markers are replicated in the test dataset, we point to one region at 4q15.2 in particular that may warrant further study.

120.57 57 New Linkage Analysis by the Autism Genome Project (AGP) Reveals Strong Evidence of Linkage to Multiple Loci as Well as Gene-Gene Interactions. J. Hallmayer*, *Stanford University*

Joachim Hallmayer representing the Autism Genetics Cooperative (AGC) and the Autism Genome Project (AGP).

Background: The AGP is an international consortium with the aim to find susceptibility genes for autism spectrum disorders (ASD). As a first step, the AGP conducted the most

comprehensive linkage study of ASDs to date; currently a Genome Wide Association Study (GWAS) is in progress using the Illumina Human 1M Bead Chip. The original linkage and CNV study (1181 multiplex families, 10K SNP data), published in Nature Genetics, yielded a peak Z_{LR} = 3.6 on 11p12-p13 in the whole data set; no other loci crossed the threshold for suggestive linkage.

Objectives: a) To reexamine the linkage data using the model-integrated posterior probability of linkage, or PPL, to account for heterogeneity by dividing the data set into subsets based on IQ status in AS individuals (Low, Normal, or Missing). b) To explore whether allowing for different male and female penetrances will substantially change the results. c) To test for gene-gene interaction between the engrailed 2 (EN2) gene and other markers in the genome

Methods: We use a quasi-Bayesian framework to reanalyze the AGP data, sequentially updating linkage evidence across data collection sites, separately for LIQ, MIQ, and NIQ families.

Results: Overall 98% of the genome shows PPL < 5%, and 90% of the genome gives evidence against linkage (PPL < 2%). In the NIQ group we find strong evidence of linkage to one locus, with 65% posterior probability of linkage (PPL) on 11p15.4-15.3; as well as PPL=24% over the original 11p12-p13 peak and 22% at 11q14.1. In the LIQ group we obtain a similarly clean plot, with several striking linkage peaks: 55% on 1q31.3, 25% on 2p25.1, 50% on 11p15.2; 32% on 11p12p-13 (the original peak), 46% on 13q22.1 (a previously implicated AD/specific language impairment locus), and 95% on 16q21. Other than the original peak on 11p12-13, there is no overlap in findings between LIQ and NIQ groups. Small but positive evidence (PPL = 3%-17%) is also seen over CNTNAP2, the 16 microdeletion region, CENTG2, the Prader-Willi/Angelman del/dup region on 15q, and the MET region on 7, all of which have been implicated in AD. Allowing for different male and female penetrances did not substantively alter the results.

We, then, incorporated genotypes for an SNP in the EN2 gene, that had been previously shown to be associated with autism, and repeated the genome scan allowing for two-locus (2L) epistasis. We find evidence of interaction with EN2 at the 15q del/dup region (2LPPL=25%) in NIQ; and strong evidence at the 11p14, p15 regions (69%, 46%) and at 13q22 (54%) in LIQ, as well as at several additional loci not detected in the single-locus scan.

Conclusions: We have obtained multiple strong linkage and epistasis signals in the largest ASD linkage study to date. Follow-up molecular work is underway, as are additional PPL analyses involving sex differences and interactions with other candidate genes.

120.58 58 A Pathway-Based Approach to Association Analysis in Autism. C. Hicks*, A. Tchourbanov, G. Steinhardt, R. Asfour and J. Del Greco, *Loyola University Medical Center*

Background: Recent advances in high-throughput genotyping have made it possible to conduct large-scale genome-wide association studies (GWAS) at population level to identify gene variants and genes associated with risk for common human diseases and a variety of psychiatric disorders such as autism. Over, the last several years many gene variants and candidate genes associated with autism have been identified using GWAS. However, the full breadth of the goals of high-throughput genotyping and GWAS to dissect the genetic architecture of autism is rapidly running into several bottlenecks in translating findings and hypothesis from GWAS to clinical practice to improve human health. One of the more significant bottlenecks is the inability of current GWAS analytic techniques to identify causal pathways and to characterize the functions of identified gene variants and candidate genes. Objectives: The objective was to determine if variation associated with autism tends to aggregate or cluster in biological pathways and gene networks. Methods: We conducted a gene and pathway-based association analysis using information from 2 genome-wide association studies to identify pathways and model gene networks involved in autism. We hypothesized that gene variants associated with autism map to and destabilize multiple candidate genes interacting within pathways and gene networks. Results: Our results show that genes containing genetic variants associated with autism are functionally related and interact with each other and their downstream targets within pathways and gene networks. Using publicly available gene expression data set, we are validating the results to infer the causal association between gene expression and autism.Conclusions: Our analysis

demonstrates that integrative genomics leveraging information from GWAS with pathway analysis provides a powerful unified approach to autism biomarker discovery.

120.59 59 Identification of Genetic Variation in Autism Using Multiplexed Massively Parallel Sequencing. A. Sekar*, J. Long, A. Kurdoglu, M. Redman, S. Walker, T. Laub, J. Corneveaux, M. Huentelman and D. W. Craig, *The Translational Genomics Research Institute*

Background:

The genetic basis of autism, in large part, is unknown and no one unequivocal susceptibility region has been identified in more than a few percent of cases. Previously, reduction of heterogeneity by examining specific sub-phenotypes of autism has resulted in stronger genetic signals. It is very likely that the autistic population with comorbid epilepsy represents a subset within the broader autism population that includes several distinct genetic insults. A common genetic link between autism and comorbid seizures has been suggested through the identification of a homozygous autosomal recessive frameshift mutation within *contactin associated protein 2 (CNTNAP2)*, which has been shown to cause a form of focal epilepsy with autistic-like language regression within the Old Order Amish population. Another gene that has been linked to autism and epilepsy is *reelin (RELN)*, which has been implicated through multiple lines of evidence.

Objectives:

To identify genetic variants in *RELN* and three members of the neurexin family, *CNTNAP1, CNTNAP 2*, and *CNTNAP4*, which are associated with autism and comorbid epilepsy, using next-generation sequencing technology.

Methods:

Multiplexed bar-coded resequencing, in which DNA barcodes are ligated to the fragments to be read, was used to simultaneously resequence a large number of samples within the same sequencing run on the Illumina Genome Analyzer. In this study, 94 individuals, 68 of whom have had at least one seizure, from the Autism Genetic Research Exchange (AGRE) cohort and 16 control samples from the National Institute of Mental Health (NIMH) collection, were resequenced across all exons from *CNTNAP1, CNTNAP2, CNTNAP4*, and *RELN*. Variants were subject to validation using capillary-based sequencing and TaqMan SNP genotyping assays. Genetic and bioinformatic techniques were used to assess the pathogenicity of the validated variants.

Results:

Exons from *CNTNAP1, 2, 4*, and *RELN*, were resequenced on the Illumina Genome Analyzer and median coverage was found to be at 40x per base across 94 individuals. Less than 10% of the originally targeted regions required additional sequencing by traditional capillary-based sequencing. Both previously identified and novel variants were found when compared to controls sequenced in this study and by aligning data from the 1,000 Genomes project. For genetic variants not found in the initial screen of controls, additional controls were screened at the variant position using ABI TaqMan assays. All novel variants identified by sequencing on the Illumina Genome Analyzer were validated when sequenced by a secondary capillary-based sequencing.

Conclusions:

The allelic spectrum of genetic variants across these genes supports that they harbor rare variants predisposing to autism with comorbid seizures.

120.60 60 Identifying Loci for the Overlap Between ADHD and PDD Using a Genome-Wide QTL Linkage Approach. J. S. Nijmeijer*[1], A. Arias-Vásquez[2], M. E. Altink[2], J. K. Buitelaar[3], C. J. M. Buschgens[2], S. V. Faraone[4], E. A. Fliers[2], B. Franke[2], R. B. Minderaa[5], N. N. J. Rommelse[6], C. A. Hartman[1] and P. J. Hoekstra[5], (1)*University of Groningen and University Medical Center Groningen*, (2)*Radboud University Nijmegen Medical Centre*, (3)*Radboud University Nijmegen Medical Centre, Nijmegen Centre for Evidence-Based Practice*, (4)*SUNY Upstate Medical University*, (5)*University Medical Center Groningen*, (6)*Karakter Child and Adolescent Psychiatry University Center*

Background: Recent studies in the general population and clinical samples have shown that Pervasive Developmental Disorder (PDD) and Attention-Deficit/Hyperactivity Disorder (ADHD) overlap, both in symptoms and in underlying genetic influences.

Objectives: In this study, the genetic basis for PDD symptoms in children with ADHD was addressed using a Quantitative Trait Locus linkage approach.

Methods: Genome wide linkage analyses were performed in the Dutch participants of the International Multi-Center ADHD Genetics (IMAGE) study comprising 365 DSM-IV combined type ADHD probands and 439 of their siblings who were part of 365 families. The total and subscale scores of the Children's Social Behavior Questionnaire (CSBQ; a measure of subtle PDD symptoms) with heritabilities >0.2 were used as quantitative traits. A total of 5407 autosomal single-nucleotide polymorphisms (SNPs) were used to run multipoint regression-based linkage analyses using MERLIN-regress software.

Results: Suggestive linkage signals (LOD≥ 2.0) were found on chromosomes 2q, 3p, 7p, 7q, and 8p. The signal on chromosome 7q11.2 overlapped for three CSBQ scales, namely the total score (LOD 2.08), and the scales addressing withdrawn behavior (LOD 3.07) and understanding of social information (LOD 2.01), respectively. The regions on chromosome 7q11 and 8p21 that we identified have previously been found for autism, and the chromosome 7p13 finding overlaps with a linkage study for ADHD.

Conclusions: Defining an ADHD subtype with PDD symptoms appears to be a valuable approach for detecting susceptibility loci for the overlap between ADHD and PDD.

120.61 61 Genetic and Expression Analyses of Serotonergic Factors in Autism. K. Nakamura*[1], T. Miyachi[2], A. Ayyappan[1], M. Tsujii[3], S. Suda[1], I. Thanseem[1], K. Tsuchiya[1], H. Matsuzaki[2], K. Yamada[4], Y. Iwayama[4], T. Toyota[4], E. Hattori[4], T. Sugiyama[5], N. Takei[1], T. Yoshikawa[4] and N. Mori[1], (1)*Hamamatsu University School of Medicine*, (2)*The Osaka-Hamamatsu Joint Reserach Center for Child Mental Development, Hamamatsu University School of Medicine*, (3)*Chukyo university*, (4)*RIKEN Brain Science Institute*, (5)*Aichi Chilren's Health and Medical Center*

Background: Autism is a neurodevelopmental disorder defined by social and communication deficits and ritualistic-repetitive behaviors, detectable in early childhood. The serotonergic system, which has an enormous influence over several brain functions, including memory, learning, mood, and behavior, has been suggested to be developmentally dysregulated in autism. Altered developmental dynamics of serotonin synthesis and elevated whole blood serotonin have been observed in autism. Serotonin is involved in various aspects of neurodevelopment that might influence anxiety-like and aggressive behaviors. Extracellular serotonin concentration is regulated by the serotonin transporter (SERT), which mediates the presynaptic reuptake of serotonin, on termination of neurotransmission. SERT is the major target of selective serotonin reuptake inhibitors, which are used in the treatment of functional impairments associated with autism. A single-photon emission computed tomography (SPECT) study reported reduced SERT binding capacity in several brain regions of autistic children compared to controls. SERT expression, and the factors that regulate the expression of SERT, might thus have a crucial role in the pathogenesis of autism.

Objectives: We carried out mRNA expression analyses and genetic association studies of the following genes that have been reported to influence the expression of SERT, (i) syntaxin 1A (*STX1A*); (ii) roundabout, axon guidance receptor, homolog 3 (*ROBO3*); (iii) integrin, beta 3 (*ITGB3*); (iv) myristoylated alanine-rich protein kinase C substrate like protein (*MacMARCKS*).

Methods: Differential expression of mRNA between control and autism samples was examined in the following postmortem brain samples obtained from Autism Tissue Project (ATP), (i) anterior cingulate (AC) (13 control, 8 autism); (ii) motor cortex (MC) (8 control, 7 autism); (iii) thalamus (9 control, 8 autism). Quantitative real-time PCR (qRT-PCR) analysis was done by TaqMan method; the fold change in gene expression between the control and autism groups was determined by calculating $2^{-DDC}{}_{T}$. Family-based genetic association studies were carried out in samples of two different ethnic origins, (i) 252 Caucasian trio samples obtained from Autism Genetic Resource Exchange (AGRE); (ii) 126 Japanese trio samples. TaqMan method was used to score SNPs, and markers were tested for association by transmission disequilibrium test (TDT).

Results: We observed altered expressions of genes in the various brain regions of autism patients as following, (i) *STX1A*: decreased expression in the AC of autism patients (p=0.008); (ii) *ROBO3*: elevated expression in the AC (p=0.028) and in the MC (p=0.038) of autism patients; (iii) *ITGB3*: elevated expression in the AC (p=0.003) and in the thalamus (p=0.039) of autism patients; (iv) *MacMARCKS*: elevated expression in the AC of autism patients

(p=0.004). We also found (i) SNP and haplotype associations of *STX1A* with autism in Caucasian and Japanese samples (ii) SNP and haplotype associations of *ROBO3* with autism in Caucasian samples. Further, *STX1A* showed association with ADI-R_D (early developmental abnormalities) and *ROBO3* showed association with ADI-R_A (social interaction) scores.

Conclusions: Several of the genes related to the serotonergic system showed altered expressions in various brain regions of autism patients compared to controls. We suggest a possible role of these genes in the pathogenesis of autism through regulation of serotonergic system.

120.62 62 Is a Functional Serotonin Transporter Polymorphism Linked to the Core Symptoms of Autism or Comorbid Psychopathology?. E. Duketis*[1], F. Poustka[1], G. Pakalapati[2], A. Benner[2], C. M. Freitag[1] and S. M. Klauck[2], (1)*Johann Wolfgang Goethe-University*, (2)*German Cancer Research Center (DKFZ)*

Background: The serotonin transporter strongly modulates serotonin function and is a major pharmacological target in the treatment of repetitive behaviour in autism as well as in the treatment of comorbid anxiety and depression. The 5-HTTLPR variant in the Serotonin Transporter Gene has been repeatedly assessed for association with autism leading to contradictory results. Recently, the functional SNP rs25531 (A/G) within the long allele (L) was described. The A variant of SNP rs25531 within the long allele (L_A) leads to higher expression, the dominant short allele (S_A, S_G) and L_G lead to lower expression of the serotonin transporter.

Objectives: We hypothesize that (1) The L_A allele of the serotonin transporter polymorphism, HTTLPR**,** alters the risk of autism and (2) the L_AL_A genotype is linked to autistic symptoms (especially repetitive behavior) and to comorbid psychopathology like anxiety, OCD and depression. Methods: (1) We performed genotyping in a German trio sample of 248 patients with autism and their parents. The transmission of the long and short alleles of the HTTLPR polymorphism including the rs25531 was investigated using the transmission disequilibrium test (TDT). (2) Additional linear regression analyses were performed to explore the influence of the L_AL_A genotype on behavioral characteristics measured by the Autism Diagnostic Interview-Revised and the Child Behavior Checklist.

Results: A trend towards higher transmission of the L_A allele of HTTLPR/rs25531 was found in the sample of autistic patients (nominal p value= .047). Within the subgroup of patients with the L_AL_A genotype (n=75) repetitive behavior was slightly increased but this difference did not reach significance (p= .13). No association with other core features of autism such as communication deficits or deficits in social interaction was observed.

Conclusions: The results indicate that the L_A allele of HTTLPR/rs25531 may play a role in the pathogenesis of autism, but – contradictory to results of previous studies - seems not to influence phenotypic variability within autism.

120.63 63 MAOA, DBH and 5-HTT Variants and Autism Spectrum Disorders in the CHARGE Samples. F. Tassone[1], L. Qi*[1], W. Zhang[1], R. L. Hansen[2], I. Hertz-Picciotto[2] and I. N. Pessah[3], (1)*UC Davis*, (2)*University of California at Davis*, (3)*M.I.N.D. Institute, University of California at Davis, CCEH*

Background: There is strong evidence that genetic factors play an important role in the development of autism.However, several research groups, often with different results, have studied a number of candidate genes, which emphasizes the complexity of the underlying etiology and pathophysiology of the disorder.

Objectives: We examined three loci, the serotonin transporter (5-HTT), the dopamine hydroxylase (DβH) and the Monoamine Oxidase A (MAOA) for association with autism using partecipants from the CHARGE Study. The CHARGE (Childhood Autism Risks from Genetics and the Environment) Study is the first large-scale population-based case-control study investigating both environmental and genetic contributions to autism risk.

Methods: The study has been recruiting families with children aged 2-5 years from three groups: autism (AU), autism spectrum disorder (ASD), and from typically developmenting (TD) controls from the general population.
We tested for association between each of the three microsatellites and autism in a sample of 128 children with AU, 61 with ASD, and 167 TD. We also conducted family-based association test transmission disequilibrium in these families (189 trio families with a child with ASD or autism and 167 families with a typically developing child).

Results: No significant transmission disequilibrium was found for any of the microsatellites in families of children with autism and ASD. This analysis was underpowered due to the preponderance of homozygous mothers in this sample, who do not contribute to transmission analyses. Based on the case-control association analysis, neither the 5-HTT nor the DBH genes showed any statistically significant association with autism. However, among White and Hispanic males, the children carrying allele 4 of the MAOA gene showed a 2-fold higher risk of AU (or AU+ASD combined) than those carrying allele 3 (multiple logistic regression adjusting for race and maternal age, 95% CI = 1.12, 3.65, p = 0.02 for AU vs. TD, and 95% CI = 1.19, 3.53, p = 0.01 for AU+ASD vs. TD).

Conclusions: These results suggest a potential role of the functional MAOA-uVNTR alleles in autism spectrum disorders.
Understanding the molecular mechanisms linked to the functional polymorphisms variants in the neurotransmitter pathways and understanding the role of the environment contribution may help to elucidate how these polymorphisms can determine the behavioral outcome.

120.64 64 Serotonin Transporter Gene Polymorphisms and Processing of Fearful Faces in Autism. E. Daly*[1], P. Johnston[2], Q. Deeley[1], L. Pugliese[2], B. Hallahan[1] and D. Murphy[2], (1)*Institute of Psychiatry, King's College London*, (2)*King's College London, Institute of Psychiatry*

Background: The characteristic social impairments found in Autistic Spectrum Disorders(ASD) may be influenced by alterations in the processing of facial emotions. Functional MRI imaging studies of people with ASD show neural hypoactivation in brain regions supporting social cognition such as the amygdala (Deeley et al. 2007). The amygdala plays an important role in the processing of fearful faces (Blair 2003). This neural activity in the amygdala is affected by the allelic variation of the serotonin transporter gene (5-HTT). The presence of one or two copies of the short allele of 5-HTT shows greater amygdalar activity when processing fearful face than in the presence of two of the long allele. Serotonin and the serotonin transporter gene are reportedly involved in he pathophysiology of ASD (Huang 2008).

Objectives: The objective of this study is to examine the influence of serotonin transporter polymorphisms on the role of the amygdala when controls and subjects with Austism process fearful faces.

Methods: 13 adults with ASD and 11 matched controls performed an event-related functional Magnetic Resonance implicit fear processing task on a GE 1.5T Signa Scanner. All participants were male, right-handed, with an IQ >70. All individuals with ASD met algorithm cut-offs for autism on the ADI or ADOS. Subjects viewed expressions of fear contrasted with a cross hair baseline condition. The BOLD signal was extracted from the left amygdala for both groups of subjects. Genotyping was performed to ascertain the allelic varation of the 5-HTT for either the short containing (SS+SL) or long (LL). Self-reporting psychiatric inventories and neuropsychological tests were performed.

Results: Genotyping revealed that the controls had 2 subjects with LL and 9 subjects with SS+SL, while the ASD group had 3 subjects with LL and 10 subjects with SS+SL. For the controls, there was a significant linear increase in amygdalar activation for the SS+SL group compared to the LL group. In contrast, subjects with ASD showed no difference dependant on 5-HTT variation.

Conclusions: These results suggest that there are variations in the influence of 5-HTT variation on the activity of the amygdale between people with ASD and controls.

120.65 65 Investigating the Relation Between Serotonin (5-HT) and Insistence on Sameness in Autism Spectrum Disorders Using Genetic and Biological Markers. S. J. Guter*[1], C. W. Brune[1], G. M. Anderson[2], J. Sutcliffe[3], E. L. Crawford[3], J. J. McElroy[3] and E. H. Cook[1], (1)*University of Illinois at Chicago*, (2)*Yale University School of Medicine*, (3)*Vanderbilt University*

Background:

The serotonergic system may play an important role in the manifestation of autism spectrum disorders (ASDs). Genetic studies using linkage and association have identified the serotonin transporter gene (*SLC6A4*) as a candidate gene for ASDs. Recent cross disciplinary research has shown that haplotypes in this region alter 5-HT levels. Biological measures of serotonin (5-HT) are correlated in relatives of individuals with ASDs. Given the utility of selective serotonin reuptake inhibitors in reducing problem behaviors attributed to restricted and repetitive behavior in ASDs, several questions exist about the relation between 5-HT and RRB. We focus on aggression

and the RRB Insistence on Sameness (IS), a potentially debilitating phenotype, first described by Kanner and now used to reduce heterogeneity in genetic studies.

Objectives:

The primary purpose of this study is to investigate the relation between 5-HT and IS using genetic and biological markers including genotypes within *SLC6A4* and whole blood platelet 5-HT. A secondary objective is to analyze the relations among the 5-HT measures and individual characteristics including age and sex in a sample with ASDs.

Methods: Individuals (N = 52, 3-27-years-old) participating in an Autism Center of Excellence study visited a university center for comprehensive diagnostic testing. Separate blood samples were drawn and analyzed for genotype and 5-HT in independent laboratories blind to sample identity. Genotyping included the functional variants (i.e. Lg, La, Sg) of the *5-HTTLPR* polymorphism and the following SNPs which may modify *5-HTTLPR* expression: rs25532, rs16965628, rs2020936, rs2020937. Whole blood platelet 5-HT was measured by HPLC with fluorescent detection. Parents completed several measures about their children including the Autism Diagnostic Interview-Revised (ADI-R) and the Repetitive Behavior Scale-Revised (RBS-R). Lifetime and current IS were characterized using items from the ADI-R factor (Cuccaro et al., 2003). Current behavior was also measured on the RBS-R Ritualistic/Sameness and Compulsive Behavior subscales (Lam & Bodfish, 2007). Aggression was measured on both instruments. Correlations between 5-HT, IS, and aggression were produced. 5-HT, IS, and aggression scores were compared across genotype groups including haplotypes. Individuals with high IS and aggression were compared to others on 5-HT measures. Lastly, extensive phenotype information will be explored for individuals who were outliers on measures of 5-HT.

Results:

Preliminary analysis included 23 Caucasian, non-Hispanic subjects free of medications which influence serotonin. One outlier with high 5-HT was excluded. Age was negatively correlated with 5-HT ($p<.01$), but none of the behavior measures. IS on the ADI-R and RBS-R were correlated ($p<.01$). 5-HT positively correlated with total score on the RBS-R ($p=.08$), but not IS. Lifetime IS scores on the ADI-R were highest for the S/S and La/La groups at *5-HTTLPR* ($p=.07$). The La/La group scored significantly higher on RBS-R Compulsive subscale ($p=.05$). The High IS with aggression group did not significantly differ on 5-HT level or *5-HTTLPR* genotype.

Conclusions: Additional analyses in a larger group will test more thoroughly whether genetic and biological markers of 5-HT relate to IS and aggression in a sample with ASDs. The preliminary findings raise interesting questions about the relation between 5-HT and IS.

120.66 66 A Pharmacogenetic Study of Escitalopram in Autism. T. Owley*, C. Brune, J. Salt, L. Walton, S. J. Guter, N. Ayuyao, R. Gibbons, B. Leventhal and E. H. Cook, *University of Illinois at Chicago*

Background: The Autism Spectrum Disorders (ASDs) are a group of neurodevelopmental disorders characterized by qualitative impairments in reciprocal social interactions, language and communication, and the presence of restricted, repetitive, and stereotyped behaviors and interests. The definitive usefulness of selective serotonin reuptake inhibitors in this population has not been determined, but some studies have suggested that SSRIs may be useful in the treatment of certain symptoms of subjects with ASDs. These symptoms include repetitive behaviors, anxiety, irritability, aggression and self-injurious behavior and more global behavior. In an attempt to determine who might have a positive response to medication, as well as help discover better dosing strategies and predict adverse effects, this study used a pharmacogenetic approach to these questions. The serotonin transporter (5-HTT) was focused on as a logical possible determinant of outcome for two reasons. First, the primary site of action of the SSRIs is the 5-HTT, where these medications act to decrease the reuptake of serotonin, increasing serotonergic signaling at the synapse. Second, polymorphisms in the promoter region of the transporter (5-HTTLPR) have been discovered that are thought to be play an important role in 5-HTT gene expression. **Objectives:** To assess the effect of escitalopram and to determine the effect of serotonin transporter polymorphism promoter region (5-HTTPLR) genotypic variation (low,

intermediate, and high expression groups) on response to escitalopram treatment of children and adolescents with Autism Spectrum Disorders (ASDs). **Methods:** The study used a forced titration, open label design, with genotype blind until study completion. Participants were children and adolescents aged 4 to 17 years of age with a confirmed ASD (Autistic Disorder, Asperger's Disorder, or Pervasive Developmental Disorder, Not Otherwise Specified). **Results:** The interaction between genotype groups and time on the Aberrant Behavior Checklist Irritability Subscale (primary outcome variable) showed a significant decrease (improvement) in scores for the intermediate and high expression genotype groups compared to the low expression group (s/s 5-HTTLPR genotype) (MMLE = -4.84, Z = -2.89, SE = 1.67, p = 0.004) followed by a plateau in ratings for all groups (MMLE = 2.01, Z = 3.09, SE = 0.65, p = 0.002). Refined expression groups based on diplotypes including intron 1 markers further clarified the low expression group and response to treatment. **Conclusions:** This genotype-blind, prospective pharmacogenetic study found the following differences in response as a function of 5-HTTLPR genotype: 1) The group of subjects with higher expressing 5-HTTLPR genotypes had a better response to pharmacotherapy than subjects with a low expressing genotype group and 2) there was a difference in the final dose by genotype groupings, with the lowest expressing genotype group having a lower final dose when compared with higher expressing genotype groups.

120.67 67 An Association Between a Functional Variant of the MET Gene and the Presence of Maternal Anti-Fetal Brain Antibodies. L. S. Heuer*[1], D. Braunschweig[1], R. Boyce[2], P. Levitt[3], D. B. Campbell[3] and J. Van de Water[2], (1)*University of California, Davis*, (2)*University of California at Davis*, (3)*Vanderbilt University*

Background: Autism Spectrum Disorder (ASD) is a highly heritable disorder. However, few causative mechanisms have been described for these genetic perturbations. Recently, a functional polymorphism in the *MET* gene ('C' allele of rs1858830) was associated with autism risk in three independent samples (P<1x10-6). The *MET* 'C' allele disrupts gene transcription and results in a ~2 fold decrease in the expression of the gene product, the MET receptor tyrosine kinase. MET signaling is involved in a number of physiological processes that are relevant to autism risk, including the formation and maturation of neural circuitry and negative regulation of immune responses. An independent line of research revealed that a subset of mothers of children with autism exhibit an inappropriate immune response in the form of antibodies directed against specific fetal brain proteins. A pattern of two specific maternal autoantibody bands, at 37 kDa and 73 kDa, was specific to mothers of children with autism. We hypothesized that mothers who are carriers of the *MET* 'C' allele may have an increased incidence of fetal-brain autoantibodies as a result of altered immune system regulation.

Objectives: To examine association of *MET* rs1858830 genotype with the presence of maternal antibodies directed against fetal brain proteins.

Methods: Genotypes at the *MET* rs1858830 locus were determined by direct re-sequencing. In addition, plasma from all mothers was analyzed by western blot for the presence of antibodies directed against specific fetal brain antigens. The presence of a 37 and 73 kDa band was then correlated with the *MET* rs1858830 genotype. Results: 100% of AU mothers harboring both the 37 and 73 kDa bands also had either the *MET* C/C or C/G genotype while none of the control mothers had this antibody pattern (P=0.005). Further, analysis of *MET* 'C' allele association with the 37 kDa band alone in the mothers with children with autism also revealed a significant association (P=0.003). There was no association of the *MET* 'C' allele with the 73 kDa band alone.

Conclusions: These results suggest that the presence of the *MET* 'C' allele in mothers of children with autism may increase susceptibility to immune dysregulation and the consequent generation of antibodies directed towards fetal brain proteins. Specific hypotheses will be tested concerning the functional effect of the *MET* gene variant on negative regulation of immune responses in mothers of children with autism.

120.68 68 Phenotypic Consequences of Misregulation of Human Chromosome 15-Associated Autism Candidate Genes in Mouse. L. Herzing*, K. Kugle, M. Yasvoina, S. Zeng and K. Varga, *Northwestern University Feinberg School of Medicine*

Background: Multiple lines of evidence implicate genes within human chromosome 15q11-q13 as contributing to autism spectrum disorders, including regional duplication occurring in approximately 2% of patients with non-syndromic autism, positive linkage association in patient populations with idiopathic autism, and aberrant

gene expression levels in both these groups and in patients with the autism spectrum disorder, Rett syndrome. The consequences of misexpression of these genes individually or collectively at the cellular and organismal level is not known.

Objectives: To determine the behavioral and neurologic consequences of misexpression of individual human chromosome 15-associated autism candidate genes in mouse.

Methods: Several mouse lines have been generated that over- or under-express candidate genes utilizing ptet-Off inducible expression vectors constructs or shRNA-mediated gene knockdown. Behavioral phenotypes were assessed in these, heterozygous gene knockout and wild-type control animals using standard protocols, including anxiety (open field), exploratory (place preference & T-maze), socialization (interest, preference & memory: tethered & free interactions) and reversal learning (radial maze).

Results: No changes have been observed to date in anxiety, exploratory or general social interest in our lines, with the exception of rare individual animals exhibiting an overall decrease in activity levels or premature death in adulthood. Preliminary data suggests that misexpression of separate candidate genes leads to abnormal trends in place-preference ($p<0.002$) or T-maze behaviors ($p<0.06$), respectively. We are currently following up these studies to more specifically define abnormal behaviors, and define their relationship to total or regional gene expression levels.

Conclusions: We provide evidence that small changes in the expression of murine genes homologous to autism candidate genes within human 15q11-q13 affect phenotypes in mouse believed to be representative of autism diagnostic criteria in humans, including social and perseverative behaviors. Aberrant expression of these genes together or individually may contribute to the development of autism spectrum disorder or of specific ASD-related features in patients.

120.69 69 Polymorphism in the DBH Promoter Region Shown to Exert Cell-Specific Effect on Transcription. L. E. Cochrane*, M. J. Hill, K. Tansey, R. J. Anney, M. Gill and L. Gallagher, *Trinity College Dublin*

Background: Autism is an early onset neurodevelopmental disorder affecting three core areas of behaviour – communication, social behaviour and restricted/repetitive behaviour. Pathophysiological studies have implicated dysfunctions in the catecholamine neurotransmitter system in the aetiology of autism. Dopamine-B-Hydroxylase (DBH) catalyses the conversion of dopamine to noradrenaline in the catecholamine pathway. Previous studies have shown altered DBH activity in individuals with autism. rs1611115, located in the *DBH* promoter region, has previously been shown to explain approximately 52% of the variance in DBH activity levels.

Objectives: This study investigated the effect of rs1611115 on *DBH* promoter function using a reporter assay system.

Methods: Inserts representing each allele at rs1611115 were inserted into the pGL3 basic reporter vector (,). Each construct was then transfected into two cell lines – CHO K1 and SH SY-5Y. Differences in promoter activity between alleles was then determined using a luciferase reporter assay system (,).

Results:

In the non-neuronal CHO K1 cell line, neither reporter construct increased relative expression levels of the luciferase reporter gene. In the neuronal SH SY-5Y cell line, both constructs increased gene expression beyond background levels. Additionally, significant allelelic differences in relative expression levels were observed ($p=0.0049$).

Conclusions:

This finding confirms at the molecular level previous reports that variation at rs1611115 affects *DBH* promoter efficiency.

120.70 70 Increased Lipid Peroxidation in Cerebellum and Temporal Cortex in Autism. A. Chauhan*[1], B. Muthaiyah[1], M. M. Essa[1], W. T. Brown[2], J. Wegiel[2] and V. Chauhan[1], (1)*NYS Institute for Basic Research in Developmental Disabilities*, (2)*New York State Institute for Basic Research in Developmental Disabilities*

Background: Accumulating evidence suggests that oxidative stress may provide a link between susceptibility genes and pre- and post-natal environmental stressors in the pathophysiology of autism. Brain tissue is highly heterogeneous with different functions localized in specific areas.

Studies on oxidative stress in relation to specific regions of the brain are lacking in autism.

Objectives: In this study, the status of lipid peroxidation was compared in postmortem brain samples from the cerebellum and frontal, temporal, parietal and occipital cortex from autistic subjects with age range of 4 to 39 yrs (N = 7-10 for different brain regions) and age-matched normal subjects (N = 9-10).

Methods: The levels of malonyldialdehyde (MDA), an end product of fatty acid oxidation, were assayed in the brain homogenates from autism and control subjects.

Results: MDA levels were significantly increased by 124 % in the cerebellum and by 256 % in the temporal cortex in autism as compared to control subjects. No overlap of MDA levels was observed in the temporal cortex between autism and control groups. In the cerebellum, 57 % of autism subjects had MDA levels above the cutoff value (upper range for control group). In contrast, no significant change in MDA levels was observed in frontal, occipital and parietal cortex between autism and control groups.

Conclusions: These results suggest that oxidative stress differentially affects selective regions of the brain, i.e. cerebellum and temporal cortex, in autism.

120.71 71 Increased Oxidative Damage in Lymphoblasts from Autism: Enhanced Free Radical Generation Coupled with Reduced Antioxidant Status. M. M. Essa*[1], B. Muthaiyah[1], V. Chauhan[1], W. T. Brown[2] and A. Chauhan[1], (1)*NYS Institute for Basic Research in Developmental Disabilities*, (2)*New York State Institute for Basic Research in Developmental Disabilities*

Background: Recent evidence suggests that autistic subjects are under oxidative stress. Most of these studies were done with serum, plasma or erythrocytes. The studies with cell cultures are lacking in autism. Under normal conditions, a dynamic equilibrium exists between the production of free radicals (reactive oxygen species - ROS) and the anti-oxidant capacity of the cell. The free radicals are highly reactive, and their elevated levels lead to oxidative stress and cell death. Antioxidants enzymes scavenge the free radicals and play vital role in the intracellular defense mechanism against oxidative damage.

Objectives: The aim was to compare the status of oxidative stress and antioxidant potential in lymphoblasts from autistic subjects (n=11) and control subjects (n=11) by analyzing lipid peroxidation, generation of free radicals (ROS), extent of membrane damage and the activities of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and glutathione reductase (GR).

Methods: The lymphoblasts from autistic and control subjects were obtained from Autism Genetic Resources Exchange Program**,** and the cell lysates were prepared. Lipid peroxidation was assessed by measuring malonyldialdehyde, an end product of fatty acid oxidation. ROS levels (basal and upon induction by Fenton reaction) were determined by using dichlorofluorescin-diacetate (DCFH-DA) as a fluorescent probe. Damage of the plasma membrane was evaluated by measuring the amount of intracellular lactate dehydrogenase (LDH) that was released into the conditioned medium. SOD activity was measured by using assay kit from Calbiochem. CAT activity was measured spectrophotometrically by analyzing complex of ammonium molybdate with H2O2. Measurement of GPx activity was based on the oxidation of GSH to oxidized glutathione (GSSG) catalyzed by GPx. Activity of GR was measured by the method based on the reduction of GSSH by NADPH.

Results: Lipid peroxidation and ROS levels were significantly increased in lymphoblasts from autistic subjects as compared with control lymphoblasts. The release of LDH, a marker of membrane damage, into the medium was also significantly increased in lymphoblasts from autistic subjects as compared with controls, suggesting that membrane integrity is affected in autism. The activities of SOD, CAT and GR, which scavenge free radicals and participate in antioxidant defense were significantly reduced in lymphoblasts from autistic subjects as compared with controls, suggesting that intracellular defense mechanisms against oxidative damage is impaired in autism. A trend towards decrease in the activity of GPx was also observed, but it was not significant.

Conclusions: Our results indicate that autism is associated with increased ROS generation along with a reduction in the activities of antioxidant enzymes, which may lead to increased oxidative damage and membrane damage in autism.

120.72 72 Sera from Children with Autism Alter Proliferation of Human Neuronal Progenitor Cells Exposed to Oxidation. B. Mazur-Kolecka*[1], I. L. Cohen[1], E. C. Jenkins[1], M. J. Flory[2], W. T. Brown[2] and J. Frackowiak[1], (1)*NYS Institute for Basic Research in Developmental Disabilities*, (2)*New York State Institute for Basic Research in Developmental Disabilities*

Background: Altered brain development during embryogenesis and early postnatal life has been hypothesized responsible for abnormal behaviors in autism. A specific genetic background that alters vulnerability to some environmental insults has been suggested in the etiology of autism; however, the specific pathomechanisms have not been identified. Recently, we showed that sera from children with autism alter maturation of human neuronal progenitor cells (hNPCs) in culture. Results suggest that regulatory factors present in sera from people with autism affect pre-programmed neurogenesis. This cell culture model of neurogenesis in autism seems to be suitable to study the effect of factors from external environment, e.g., oxidative stress that is putative risk factor in autism.
Objectives: To evaluate the susceptibility of hNPCs to oxidative stress during different stages of neuronal differentiation in an "autistic environment", i.e., stimulated with sera from children with autism. Methods: Neurospheres of hNPCs were exposed to a mild oxidative stress--non-cytotoxic concentrations of ferrous ions--applied at the beginning and during differentiation induced by sera from children with autism and controls at different ages. Apoptosis was evaluated based on morphology of cellular nuclei, DNA fragmentation and Bcl2 expression. Proliferation of hNPCs was tested using incorporation of bromodeoxyuridine during a 2 h pulse. Neuronal development was estimated by expression of specific markers by immunocytochemistry and Western blotting. Results: Treatment with a 200μM solution of ferrous ions did not increase the mortality of hNPCs, apoptosis and formation of carbonyls—a marker of oxidative protein damage. Proliferation of cells was affected by the treatments, as was examined in a three-way ANOVA in which autistic status, age and schedule of the exposure to ferrous ions were entered as factors. The overall ANOVA was significant ($F(15\ df)=23.6$, $p < .001$). Age of serum donors was marginally significant ($F(1\ df) = 4.01$, $p = .047$), and stage of cell differentiation during treatment was highly significant ($F(3\ df) = 103.5$, $p < .001$). The degree of proliferation was affected by autistic status to a different degree among the experimental groups ($F(3\ df) = 8.31$, $p < .001$). Post-hoc comparisons showed significant differences between the cultures in which ferrous ions were or were not added during differentiation of neuronal progenitor cells ($p < .001$). Pairwise ANOVAs revealed that the effect differed between the autistic and control groups. The treatments did not influence expression of neuronal markers during 48 hours of culture.
Conclusions: (1) Factors present in sera of autistic children altered the sensitivity of differentiating hNPCs to a mild oxidative stress. Results suggest that oxidative stress may affect renewal and development of NPCs in autism. (2) hNPCs exposed to factors present in autistic sera may be a useful model to study the pathomechanisms of environmental risk factor that affect neurogenesis and brain plasticity leading to altered behavior in autism.

120.73 73 Monocyte Cytokine Responses to TLR Ligands in Children with ASD. A. M. Enstrom*[1], J. Van de Water[2], I. N. Pessah[3] and P. Ashwood[1], (1)*M.I.N.D. Institute, University of California at Davis*, (2)*University of California at Davis*, (3)*M.I.N.D. Institute, University of California at Davis, CCEH*

Background:

Increasing evidence has suggested that dysregulation of the immune system occurring prenatally or in early childhood may contribute to the development of autism spectrum disorders (ASD). We hypothesize that innate immune mechanisms may be abnormal in ASD and lead to inappropriate response to specific bacterial and viral antigens. Furthermore, failure of peripheral monocytes to trigger immune responses appropriately could result in ongoing inflammation that could contribute to peripheral immune dysfunction and microglial inflammation in the brain.

Objectives:

We examined the response of isolated monocytes to specific viral and bacterial ligands in children diagnosed with ASD compared to typically developing control children who were enrolled in the CHARGE study at UC Davis.

Methods:

Peripheral blood from 17 children with ASD (average age 3.9 years) and 16 typically developing children (average age 3.3 years) was isolated and mononuclear cells obtained by

density gradient centrifugation. CD14+ monocytes were isolated by magnetic bead separation and stimulated for 24 hours with specific toll-like receptor (TLR) ligands: lipoteichoic acid/LTA (TLR2), poly I:C (TLR3), lipopolysaccharide/LPS (TLR4), flagellin (TLR5), or CpG-B (TLR9). Supernatants were harvested from the cell cultures and the production of IL-1β, IL-6, TNFα, MCP-1, and GM-CSF were determined by Luminex analysis.

Results:

The production of the proinflammatory cytokine IL-1β was **increased** in monocyte cell cultures from ASD children compared to typically developing controls following stimulation with LTA (p=0.02) or LPS (p=0.04). Further, the proinflammatory cytokines TNFα and IL-6 were also significantly **increased** in monocyte cell cultures from ASD compared to controls following LTA stimulation. However, stimulation with flagellin and poly I:C did not produce differential production of these cytokines in monocyte cell cultures from ASD children compared to controls. Conversely, CpG stimulation produced **decreased** IL-β, IL-6, GM-CSF and TNFα in monocyte cell cultures from ASD children compared to controls (p<0.05). Similarly, production of the chemokine MCP-1 was **decreased** two-fold in monocyte cell cultures from ASD children following stimulation with poly (I:C) (p=0.006) or CpG (p=0.002).

Conclusions:

These results demonstrate a differential cytokine response upon stimulation of monocyte cell cultures with some TLR ligands between children with ASD compared to typically developing controls. Furthermore, these differences are associated with the specific nature of the antigen presented, suggesting that separate signaling pathways within monocytes may be affected. As monocytes are key regulators of the immune response, dysfunction in these cells could result in long-term immune alterations in children with ASD. Furthermore, as monocytes share lineage and functional similarity with microglial cells, these findings may parallel similar responses of microglial cells in the brains of children with ASD. Overall, these data suggest that monocyte cell cultures from children with ASD have changes in signaling via select TLRs when compared to age matched controls that may be indicative of an altered neuroimmune network.

120.74 74 Early Behavioral Intervention with Juvenile C57BL/6J Cagemates Improves Sociability in the BTBR Mouse Model of Autism. M. Yang*, M. Weber, K. Perry and J. N. Crawley, *National Institute of Mental Health, National Institutes of Health*

Background: Abnormal reciprocal social interaction is the primary defining symptom of autism. While there is no known effective medical treatment for the autism symptoms, well-structured behavioral interventions produce beneficial effects. Notably, peer-mediated intervention has been found to improve social skills in some children with autism, indicating the important role of frequent social interaction with social peers as part of the behavioral treatment program. BTBR T+tf/J (BTBR) is an inbred strain of mice that displays prominent social deficits as juveniles and adults, reduced social transmission of food preference, unusual patterns of vocalization, and high levels of repetitive self-grooming, symptoms with considerable face validity to the three diagnostic symptoms of autism. In the social approach test, C57BL/6J (B6) mice exhibit high levels of sociability whereas BTBR mice score poorly, indicating that these two strains might be used to test the effects of peer-mediate behavioral treatments in a mouse model of autism. Moreover, previous cross-fostering studies showed that BTBR mice raised by C57BL/6J (B6) mothers do not show improved social scores as juveniles and adults, indicating that the early postnatal maternal environment is not sufficient to alter the autism-like behaviors in BTBR.

Objectives: The present study investigates whether living with B6 juveniles in the home cage, during a juvenile to adulthood period in BTBR, could improve social approach behaviors in BTBR. Secondly, this study aims to investigate whether BTBR continue to show improved social behaviors after their former B6 cagemates have been removed.

Methods:

The intervention procedure began by forming mixed-strain cage mates. Two BTBR and two B6 of the same sex were paired at the time of weaning (postnatal day 21) and allowed to interact freely as cage mates. Control pairings 4 B6 of the same sex in the same home cage during the same

period, and 4 BTBR of the same sex in the same home cage during the same period. Animals were tested for social approach at 8 weeks of age. Subsequently, after the first social approach test at 8 weeks, BTBR mice from mixed-strain cages were separated from B6 cage mates and tested for social approach again 30 days later.

Results:

Results showed that BTBR exhibited significant sociability after living with B6 cagemates for 40 days, similar to control B6. BTBR living with BTBR cagemates for 40 days did not show sociability. Moreover, BTBR from mixed-strain cages continued to show significant sociability after living for 30 days without their former B6 cagemates, indicating long-lasting beneficial effects of the juvenile behavioral intervention strategy.

Conclusions:

Findings of the current study indicate that the profound social deficits in BTBR are significantly improved by constant social interaction with highly social B6 "peers", suggesting that the BTBR mouse model of autism could be used to explore intervention strategies to improve autism-relevant symptoms.

120.75 75 Behavioral Effects of Acute Administration of Risperidone and MPEP in the BTBR Mouse Model of Autism. J. L. Silverman*, C. L. Barkan, S. S. Tolu and J. N. Crawley, *National Institute of Mental Health, National Institutes of Health*

Background: Animal models provide research tools for evaluating proposed treatments for autism. BTBR T+tf/J (BTBR) is an inbred strain of mice that displays behavioral phenotypes with analogies to all three of the diagnostic symptoms of autism, including well-replicated social deficits, unusual patterns of vocalization, and high levels of repetitive self-grooming. These phenotypes offer straightforward behavioral assays to test pharmacological compounds.
Objectives: Pharmacological rescue of the repetitive self-grooming behavior and the social deficits in BTBR mice.
Methods: Adult male and female BTBR and control C57BL/6J (B6) mice were bred in our animal facility and tested in compliance with NIH guidelines for the care and use of laboratory animals. On the day of testing, cages of the subject mice were acclimated to the testing area for 1 hour. Subject mice were administered an intraperitoneal (i.p.) injection of risperidone (0.125 mg/kg, 0.25 mg/kg, or 0.5 mg/kg, Sigma Aldrich, St Louis, MO), MPEP (0.5 mg/kg, 1.0 mg/kg, 10 mg/kg, 30 mg/kg, Sigma Aldrich, St Louis, MO), or saline vehicle and are returned to their home cages for thirty minutes. Each mouse was then tested in one of three behavioral tasks. The social approach task was performed as previously described (Yang et al., 2007), in which approach to a novel object in one side chamber and to a novel mouse in the other side chamber were automatically recorded. Time spent sniffing the novel mouse and novel object was scored with a stopwatch by an observer blinded to drug treatment. Self-grooming behavior was assessed in subjects by placing the mouse in a clean standard mouse cage for a 10 minute habituation period and then a 10 minute test session during which cumulative time spent in self-grooming was scored with a stopwatch. The third task quantified general locomotor activity in a novel open field (AccuScan Instruments, Columbus, OH), as a control measure to detect any confounding behavioral sedation induced by the drug treatments.
Results: Low doses of risperidone significantly reduced repetitive self-grooming behavior in BTBR mice. However, a significant reduction in open field locomotion was seen at doses of risperidone that reduced self-grooming. No significant improvements in social approach were observed after acute risperidone treatment. Preliminary data indicate that MPEP significantly reduced repetitive self-grooming at doses that did not affect open field locomotion. Social approach testing following treatment with acute MPEP is in progress.
Conclusions: Our results indicate that acute treatment with MPEP, an mGluR5 antagonist, may reverse a repetitive behavioral phenotype in the BTBR mouse model of autism. Reductions in repetitive self-grooming by risperidone appears to be due to the sedating effects of acute risperidone in mice. Chronic low-dose treatments with risperidone and MPEP will be important in the future, for understanding the potential efficacy of these two classes of compounds in autism-related behaviors. The BTBR mouse model appears to offer a straightforward preclinical model for discovering treatments that rescue mouse behaviors analogous to the diagnostic symptoms of autism.

120.76 76 Comprehensive Behavioral Phenotyping of BDNF-Overexpressing Transgenic Mice. C. L. Barkan*, J. L. Silverman, S. S. Tolu and J. N. Crawley, *National Institute of Mental Health, National Institutes of Health*

Background:

Brain-derived neurotrophic factor (BDNF) is a signaling molecule involved in brain development, including aspects of neuronal differentiation, synapse formation, dendritic spine morphology, and axonal growth. BDNF has been implicated as a target in numerous neurological diseases. Autism is a neurodevelopmental disorder believed to have a strong genetic component. It is characterized by aberrant reciprocal social interactions, impaired communication, and repetitive behaviors. Unusual levels of BDNF have been reported in several autism studies, particularly during early development.

Objectives:

In order to better understand the role of BDNF in autism, we are conducting comprehensive behavioral phenotyping on a line of the BDNF-overexpressing mice as well as correlative BDNF protein expression analysis.

Methods:
Mice with the BDNF transgene expressed on a forebrain CaMKII promoter (Huang et al., 1999) were purchased from JAX (Bar Harbor, ME). Comprehensive behavioral testing of general health, reflexes, motor activity, social behavior, anxiety-like behavior, and learning and memory abilities was conducted on BDNF-overexpressing mice and their wildtype littermates as routinely conducted in our laboratory and previously described (Bailey et al, 2007; Chadman et al., 2008). Juvenile play was recorded at day 21, prior to weaning. All other behavioral tests were conducted on animals age 6-8 weeks.

Results:

Data indicate that BDNF-overexpressing mice are similar to their wildtype littermates on standardized measures of general health, neurological reflexes, motor activity, and social behavior. However, there were subtle differences in anxiety-like behaviors between BDNF-overexpressing mice and their littermates. Additionally, deficits in the cued component of cued and contextual fear conditioning in the BDNF-overexpressing mice were observed which may indicate a mild learning impairment. Currently, we are assessing performance on the Morris water maze spatial learning task, and conducting BDNF protein expression analysis for correlations with behavioral scores.

Conclusions:

Behavioral phenotyping has revealed only minor differences between BDNF-overexpressing transgenic mice and their wildtype littermates, suggesting that overexpression of BDNF does not significantly impact general health, neurological reflexes, motor abilities, juvenile reciprocal social interactions, or adult social approach in mice. However, forebrain BDNF-overexpression may influence anxiety-like behaviors and learning. In connection with this, previous work reported that αCaMKII overexpression impaired retrieval of object recognition and fear-related memory (Cao et al., 2008). Further studies in progress will investigate the hypothesis that excess forebrain BDNF affects synaptic plasticity relevant to cognitive functions, including social cognition.

120.77 77 Mouse Ultrasonic Vocalization Analyses to Model Communication Deficits in Autism. M. Wöhr*[1], M. Yang[1], F. I. Roullet[1] and J. N. Crawley[2], (1)*Laboratory of Behavioral Neuroscience, National Institute of Mental Health, USA*, (2)*National Institute of Mental Health, National Institutes of Health*

Background: Delayed language and poor communication skills are fundamental to the diagnosis of autism. Mice utter distinct types of ultrasonic vocalizations, which differ depending on the animal's age, its current affective state, and environmental factors. Infant mice emit ultrasonic vocalizations when isolated from their dam and litter. It is known that such ultrasonic vocalizations serve communicative purposes, since they elicit the mother's exploratory behavior, facilitating her retrieval of isolated pups. Furthermore, it was shown that isolation-induced ultrasonic calling in mouse pups is dependent on the social context (Branchi et al., 1998; Oswalt & Meier, 1975). We are investigating the nature of the vocalizations emitted by pup, juvenile, and adult mice in various social situations, for subsequent applications to mouse models of autism.

Objectives: The objective of the present study was to test whether the social context affects isolation-induced ultrasonic vocalizations in mouse pups and adults. Optimized methods are being tested

with the inbred strain BTBR T+tf/J (BTBR), a mouse model of autism with well-replicated social deficits, unusual calls, and repetitive behaviors, as well as in knockout mice with mutations in candidate genes for autism.

Methods: Isolated mouse pups were compared for quieting responses. To induce ultrasonic calling, 2-12 day old pups were removed from the home cage for 5 min at room temperature. Half of the litter was tested in clean bedding and the other half in soiled bedding from the home cage, which contained maternal odor. In a second paradigm, vocalizations were recorded in adult male mice in an open field containing an aliquot of adult female urine. Ultrasonic vocalizations were monitored with a CM16 ultrasound microphone, recorded by Avisoft-RECORDER and analyzed with Avisoft-SASLabPro (Avisoft Bioacoustics, Germany). Experiments were conducted in each social situation to compare C57BL/6J (B6), a highly social inbred strain of mice, with BTBR, and to compare mutant lines of mice with their wildtype littermates.

Results: When isolated from dam and litter, both B6 and BTBR pups vocalized. BTBR pups vocalized more than B6 pups, as previously reported (Scattoni et al., 2008). Preliminary data indicate that B6 displayed quieting in the presence of their home cage litter containing maternal odors, while BTBR did not. When placed in an open field containing female urine, ultrasonic vocalizations were emitted by some, but not all, male mice. Preliminary data indicate that some individuals consistently call and some individuals consistently do not call, when tested in repeated sessions.

Conclusions: Ultrasonic vocalizations appear to differ between individual mice and between strains of mice. Early results employing these two social situation tasks suggest that analyses of mouse vocalizations may offer assays relevant to communication deficits in autism.

120.78 78 Epigenetic Interaction Between Mecp2 and Organic Pollutants in Murine Development. R. O. Vallero*[1], J. K. Suarez[1], R. Woods[1], T. A. Ta[1], M. S. Golub[2], R. Berman[1], I. N. Pessah[3] and J. M. LaSalle[1], (1)*UC Davis School of Medicine*, (2)*UC Davis*, (3)*M.I.N.D. Institute, University of California at Davis, CCEH*

Background: Rett syndrome (RTT) is a neurodevelopmental disorder caused by mutations in the X-linked gene *MECP2* that encodes methyl CpG binding protein 2. MeCP2 is a known epigenetic modulator of gene expression required for postnatal neuronal maturation. In previous studies, *Mecp2*-deficient mice showed delayed neuronal maturation exhibited by alterations to the level and localization of histone H3K9 acetylation, an epigenetic marker of gene activity. Also, 80% of autism brain samples showed decreased MeCP2 expression and exhibited similar alterations to H3K9 acetylation patterns in cortical neurons. RTT is one of several neurodevelopmental disorders with a known genetic cause of epigenetic abnormalities, highlighting the importance of epigenetic mechanisms in postnatal brain development. However, neurodevelopmental disorders which have unknown genetic etiologies such as autism and mental retardation are likely to be caused by a combination of genetic and environmental factors. The recent increase in the incidence of autism cases suggests that environmental factors may play a role. The widespread use of persistant organic polybrominated diphenyl ethers (PBDEs) as commercial flame retardants over the past decade has raised concern about human exposure to this new pollutant and potential effects on the developing brain.

Objectives: This study aims to test the hypothesis that perinatal exposure to brominated diphenyl ether 47 (BDE-47) affects the development of social and cognitive behavior through epigenetic changes in neurons during development in a mouse model genetically susceptible to an autistic phenotype.

Methods: Heterozygous *Mecp2*$^{308/+}$ dams were exposed orally via cornflake to either vehicle control (corn-oil), 0.03 mg BDE-47/kg/day, or 0.1 mg BDE-47/kg/day for a 10-week perinatal period (4 weeks prior to mating, 3 weeks in utero, 3 weeks lactation). Dams were bred to wildtype males in order to yield four possible genotypes per treatment group – *Mecp2*$^{+/+}$, *Mecp2*$^{308/+}$, *Mecp2*$^{+/y}$, *Mecp2*$^{308/y}$. The pups undergo behavioral testing throughout development until approximately pnd70 when they are sacrificed and their tissues are collected. A tissue microarray was constructed consisting of triplicate 6um cores from each of the various genotypes and treatment groups. Immunofluorescence staining was performed and laser scanning cytometry (LSC) was used to quantify changes in histone acetylation and MeCP2.

Results: The 0.1 mg BDE-47/kg/day exposure negatively impacted fertility and litter survival specifically in *Mecp2*-mutant but not wild-type C57Bl6/J mice, suggesting an increased genetic susceptibility of *Mecp2*-mutant mice to BDE-47 in reproductive success. Preliminary behavioral studies on pups from 0.03 mg BDE-47/kg/day exposed *Mecp2*$^{308/+}$ dams indicate significant defects in at least one measurement of social behavior (ultrasonic vocalizations) but no changes in growth, reflex, and motor skills. Preliminary immunofluorescence and LSC data have shown changes in the levels of MeCP2 and histone acetylation in cerebral cortical neuronal nuclei in BDE-47 exposed mice influenced by *Mecp2* genotype.

Conclusions: Perinatal exposure to low doses of the organic pollutant BDE-47 combined with genetic susceptibility alters epigenetic patterns in maturing neurons and ultrasonic vocalizations in mice.

120.79 79 Autistic-Like Behaviors in GAP-43 Deficient Mouse That Displays Disordered Connectivity and Autism-Related Gene Expression. K. J. Zaccaria*[1], D. C. Lagace[2], E. A. Kelly[3], A. J. Eisch[4] and J. S. McCasland[1], (1)*SUNY Upstate Medical University*, (2)*University of Ottawa*, (3)*University of Rochester SMD*, (4)*University of Texas Southwestern Medical Center*

Background: Autism spectrum disorder (ASD) is a complex neurological disorder involving impaired social interactions, communication deficiencies and a tendency toward rigid, repetitive behaviors. An emerging theory of ASD proposes that disordered connectivity is responsible for the development of autistic behavior. Growth associated protein 43 (GAP-43) is important for normal axon targeting and stabilization of productive axonal contacts. A mouse lacking one copy of the GAP-43 gene (HZ) shows multiple abnormalities in long axonal projections. In addition, neonates show overgrowth of the somatosensory cortex. Adults recover normal cortical dimensions but display enlarged excitatory receptive fields. These findings are evidence that the GAP-43 HZ mouse is a model of disordered connectivity. Importantly, GAP-43 HZ mice also have altered expression of more than 100 genes implicated in ASD, including Fragile X, Reelin, MECP2, UBE3A, GABARB3, Wnt2, Dishevelled 1, and Engrailed 2. Thus, deletion of a single GAP-43 allele creates an autistic-like gene expression pattern in an environment displaying disordered connectivity.

Objectives: Since GAP-43 HZ mice display disordered connectivity and autistic-like gene expression, our objective was to examine its behavioral phenotype. We hypothesized that GAP-43 HZ mice would display specific autism-like behavioral deficiencies.

Methods: We tested this hypothesis with behavioral tasks designed to assess face validity in mouse models of autism. Tests included t-maze, Morris water maze, open-field object recognition, social approach, juvenile interaction, elevated-plus maze, light-dark box, forced swim test, tail suspension test, fear conditioning, and social transmission of food preference.

Results: We found that GAP-43 HZ mice show deficiencies in reversal learning (resistance to change). We also found gender-specific increases in anxiety and stress-induced behavioral withdrawal, as well as deficiencies in spatial habituation and learning. To date, we have not found significant deficiencies in social interaction or social communication.

Conclusions: We conclude that disordered connectivity and autism-like gene expression in GAP-43 HZ mice may be associated with some, but not all, mouse behaviors that exhibit face validity with symptoms of ASD.

120.80 80 Fine-Tuning the Mouse Forebrain by HGF/SF-Met Signaling. G. J. Martins*, E. A. Leumas and E. M. Powell, *University of Maryland School of Medicine*

Background: Integrating activity across various brain regions is critical for supporting adaptive behavior. Recent research has suggested that organization of neural circuitry may be affected in autism. The hepatocyte growth factor/scatter factor (HGF/SF) and its receptor, Met, have been genetically linked as autism susceptibility loci and further implicated in the development of the mouse forebrain. HGF/SF, when bound to Met, induces a signaling cascade that can act as a chemoattractant, or a general promoter of cell movement, proliferation, or differentiation in neural tissues.

Objectives: HGF/SF and Met are known to be expressed in the developing telencephalon and alterations in HGF/SF or Met expression appear to modulate proliferation and migration patterns of neurons. This study employed multiple lines of mutant mice to understand how changes in

HGF/SF-Met signaling lead to alterations in neural circuitry and behavior.

Methods: These studies employed transgenic mutant mouse lines with immunohistochemical, biochemical and anatomical studies to explore mechanisms of neural development. In addition, behavioral testing in adult animals investigated whether developmental perturbations led to long term anxiety and learning and memory dysfunction.

Results: GABAergic interneuron numbers in the adult forebrain are regulated by embryonic levels of HGF/SF-Met signaling. Furthermore, the loss of Met signaling results in aberrantly splayed thalamocortical axon tracts and tortuous pyramidal neuron dendrites possibly leading to mistargeting of signals in the cerebral cortex and abnormal neural circuit formation. Targeted mutations lead to specific behavioral problems including seizures and procedural learning.

Conclusions: Our data suggest that *Hgf* and *Met* are required in the embryonic mouse forebrain for the proper development of various systems that are integral to proper neural circuitry formation. Such disruptions can lead to profound neurological and behavioral consequences such as those portrayed in autism spectrum disorders.

120.81 81 Reduced Excitability of Intrinsic Neuronal Properties during Development of the Medial Prefrontal Cortex in a Rodent Autism Model. E. C. Walcott* and N. S. Desai, *The Neurosciences Institute*

Background:

One of the few known risk factors for autism is maternal exposure to valproic acid (VPA) during the first trimester of pregnancy. VPA is an anticonvulsant drug that is often prescribed for migraine and bipolar disorder in addition to epilepsy. An established rodent model in which pregnant rats are injected with a single dose of VPA at the time of neural tube closure results in offspring that exhibit both neuroanatomical and behavioral abnormalities similar to those observed in autistic humans. Therefore this model provides a useful tool for understanding the developmental biology of autism, and has not yet been fully explored. One remaining unexplored area of interest is the development of functional properties in the medial prefrontal cortex, an area that has been implicated in autistic dysfunction.

Objectives:

In this project we have used the VPA rat model to study how fetal VPA exposure affects the development of intrinsic neuronal properties in the medial prefrontal cortex with the goal of understanding what abnormalities may exist, and whether any observed abnormalities are present close to birth or as a result of developmental programming gone awry. Upon discovering differences in the model animals the goal is now to identify the underlying mechanisms.

Methods:

We performed whole cell patch clamp recordings from layer 2/3 pyramidal neurons in slices of postnatal rat brains (P4-P38) to characterize how passive and active electrical properties evolve beginning shortly after birth and continuing on into adulthood. Our two groups of animals consist of the experimental VPA pups and age matched saline-exposed control pups.

Results:

Our data indicate that passive properties, including resting potential, resting input resistance, and membrane time constant, developed normally in the VPA-exposed animals. Active properties, however, were impaired compared to the neurons from control animals. Neurons from the youngest VPA animals (<2 weeks) were markedly less excitable than the saline controls. Specifically, two properties that affect action potential firing, namely threshold potentials and rheobase currents, were higher while the number of action potentials generated by current steps was lower. These differences decreased over development such that responses to current steps were indistinguishable between VPA and control recordings in older animals (> 1 month).

Conclusions:

We conclude that VPA either induced a developmental delay in intrinsic properties of medial prefrontal layer 2/3 pyramidal neurons or caused an alteration in an ion channel current mediating action potential firing and homeostatic mechanisms were triggered so that these cells appeared "normal" by one month. One limitation of our techniques thus far is that simple DC current steps may not fully reveal the functional

properties of these neurons. We are currently using other methods (such as dynamic clamp simulations) to probe the older neurons with more complex stimuli to determine what, if any, differences persist. In addition, we are pursuing the cause of the observed differences by using Western blot analysis of ion channel proteins and electrophysiological isolation of specific ion channel currents.

120.82 82 The Role of Neurotensin in An Animal Model of Self-Injurious Behavior. A. M. Van Matre*, S. Wolfman and D. P. Devine, *University of Florida*

Background: The most debilitating of all the maladaptive behaviors in autism is self-injurious behavior (SIB). SIB consists of stereotyped behaviors that can produce physical injury (e.g. head-banging, face-punching, self-biting). Pemoline, an indirect monoamine agonist, produces stereotyped self-biting in rats and is used as an animal model of human SIB. Neurotensin is a neuropeptide that interacts with dopamine and glutamate, two neurotransmitter systems that we and others have identified as being important mediators of SIB.
Objectives: We are investigating the role of neurotensin in the expression of SIB and evaluating the efficacy of a neurotensin agonist (PD149163) to reduce SIB, using the pemoline model in rats.
Methods: In experiment 1, male Long Evans rats were administered either pemoline (150 mg/kg) or peanut oil vehicle each day for five days (10 rats per group). On the sixth day the rats were killed, their brains removed, and the striatum and ventral tegmentum were rapidly dissected. A neurotensin RIA (Phoenix Pharmaceuticals) was used to measure neurotensin content within these structures. In experiment 2, rats received daily injections of pemoline (150 mg/kg/day; s.c.) and either 0, 0.01, 0.1, 1.0 mg/kg of the neurotensin 1 receptor agonist, PD149163 (s.c.), twice daily for five days. SIB was measured by quantifying the duration of self-injurious oral contact with the skin and by measuring the size of injured tissue.
Results: In experiment 1 we found that neuronal content of neurotensin in the striatum was higher in pemoline-treated rats (i.e. the self-injurers) than in vehicle controls. Although not directly evaluated in this study, previous studies have shown that similar increases in neurotensin content after administration of other psychostimulants is due to decreased release of neurotensin. No differences in ventral tegmental neurotensin content were found between pemoline- and vehicle-treated rats. Experiment 2 (studying the effects of the neurotensin 1 receptor agonist on pemoline-induced SIB) is in progress and results will be reported at the conference.
Conclusions: Although our investigations into the role of neurotensin in pemoline-induced SIB are still on-going, we suggest that targeting neurotensin neurotransmission may be a clinically relevant pharmacotherapeutic tool to reduce human SIB. Furthermore, neurotensin has been described as an endogenous antipsychotic and neurotensin agonists have recently received attention for their pro-cognitive and anxiolytic effects, which further highlight the potential of neurotensinergic drugs to improve the core symptoms of autism.

120.83 83 Maternal Immune Activation during Pregnancy Alters Development of T Helper Cell Subsets of Offspring in Prenatal Models of Autism. M. Mandal*[1], A. Marzouk[2], G. Yehia[2], R. Donnelly[2] and N. M. Ponzio[3], (1)*UMDNJ - Graduate School of Biomedical Sciences*, (2)*UMDNJ - New Jersey Medical School*, (3)*UMDNJ - New Jersey Medical School & Graduate School of Biomedical Sciences*

Background: Autism spectrum disorder (ASD) is a perinatal developmental disorder characterized by behavioral, neurological, and immunological abnormalities. ASD is a multifactorial disorder, the causes of which have not been fully defined. However, clinical and experimental studies indicate that in addition to genetic predisposition, immune mechanisms, in general, and cytokine dysregulation, in particular, are contributing etiological factors in ASD. In murine models of autism, injection of pregnant dams with cytokines (IL-2, IL-6) or polyclonal activators (poly I:C, LPS) at mid-gestation causes autism-like behavioral abnormalities in their offspring in comparison to offspring of control PBS-injected dams.

Objectives: To examine murine prenatal models of autism to determine if immunostimulation during pregnancy causes alterations in the development and/or function of lymphoid and myeloid lineages in offspring, with particular emphasis on analysis of T helper subsets.

Methods: In the first model, we administered five daily i.p. injections (0.4 ug) of murine IL-2 to pregnant SJL/J mice during mid-gestation (E12-E16). In second model, C57BL/6 (B6) dams were given one i.p. injection of 20 mg/kg poly I:C (pI:C) or IL-6 (0.5 ug) at E12. Spleen cells from offspring of immunostimulated dams (IL-2, IL-6,

and pI:C pups) were compared to offspring of pregnant mice injected with vehicle only (PBS pups) for mixed lymphocyte reaction (MLR) and cytotoxic T lymphocyte (CTL) function. Multi-color flow cytometry (FACS) analysis and TH cell differentiation cultures were also performed on spleen cells from pI:C and IL-6 pups, respectively. Sera and amniotic fluids from pregnant dams and supernatants from activated lymphocyte cultures of offspring were analyzed for the presence of multiple cytokines by Luminex assay.

Results: In these well-characterized prenatal mouse models of autism, we observed high levels of pro-inflammatory cytokines in maternal sera and amniotic fluids, and changes in the T cell subsets of their offspring. In the model where SJL dams were injected with IL-2 (vs. PBS), in addition to their previously shown abnormal behavior, IL-2 pups also exhibited accelerated T cell development, with a skewing toward TH1 cell differentiation, and significantly higher MLR and CTL responses to syngeneic B lymphoma cells or allogeneic spleen cells. In the second model, 24 hrs after injection of pregnant B6 dams with pI:C (vs. PBS), high levels of pro-inflammatory cytokines were detected in the sera and amniotic fluids. In addition, FACS analysis of activated T cells from 2-3 week old pI:C pups showed higher percentages of CD4+ TH cells with intracellular IL-17 (TH17 cells) than neonates from PBS-injected dams. Naïve CD4+ TH cells from IL-6 (vs. PBS) pups also showed significantly greater ability to differentiate towards TH17 cells.

Conclusions: Maternal immune activation during pregnancy caused production of cytokines that crossed the placenta and promoted the development of pro-inflammatory TH1 and TH17 cells in their offspring. Since TH1 and TH17 cells have each been shown to mediate pathogenesis of autoimmune disease, their presence in the offspring of IL-2, IL-6, and pI:C-injected pregnant dams suggests that TH1 and TH17 cells may contribute to the immunological and behavioral abnormalities observed in these rodent models of autism.

120.84 84 Maternal Viral Infection Alters the Social and Anxiety-Like Behaviour of the Offspring. L. A. Wollaston*, G. Hall and J. A. Foster, *McMaster University*

Background: Early immune challenge during critical periods of development may influence the trajectory of CNS development. In particular, viral challenge in utero has been shown to result in molecular and behavioural changes in the offspring. In the present study, we examined the impact of prenatal immune activation using the viral mimic, polyriboinosinic-polyriobytidilic acid (Poly I:C) on the development of autistic-like behaviours over the lifespan in mice. Objectives: The objective of these experiments was to examine both social behaviour and anxiety-like behaviours following exposure to poly I:C in utero. Methods: Pregnant dams (CD1 mice) were given an i.p. injection (5mg/kg) of Poly I:C or saline on embryonic day 10. Social behaviour of the pups was assessed on postnatal day 17 (P17) and 12 weeks of age using a three-chamber apparatus. In this 2-stage testing paradigm, variation in frequency of interaction ("sociability") to a stranger mouse was tested and followed by an assessment of frequency of interaction to a familiar vs. stranger mouse (social novelty). Locomotor and exploratory behaviour was assessed at P25 using activity chambers. Anxiety-like behaviour was also assessed at 6 weeks of age using the elevated plus maze (EPM). Results: Our social behaviour analysis revealed an early deficit in both sociability and social novelty at P17, whereas at 12 weeks of age Poly I:C mice showed normal sociability and social novelty. While no differences were apparent in exploratory or locomotor activity at P25, we did observe increased anxiety-like behaviour in Poly I:C mice at 6 weeks of age. These data show that maternal immune challenge leads to alterations in the developmental behavioural trajectory of offspring in both socialbility and anxiety. The observed preweaning deficits in social behaviour in Poly I:C mice are concurrent with the critical developmental period for the emergence of anxiety-like behaviour in mice. Conclusions: Together with the observed increase in anxiety-like behaviour during adolescence, these findings suggest a link between the development of social behaviour and the molecular substrate underlying the emergence of anxiety-like behaviour. We plan to investigate the molecular signature underlying this behavioural phenotype. This work may provide important insights regarding the inter-relationship between co-morbid anxiety and social deficits in autism and changes in this dynamic across development.

120.85 85 Characterization of Maternal Plasma Antibodies to Fetal Brain in Autism. D. Braunschweig*[1], R. Boyce[1], P. Ashwood[2] and J. Van de Water[1], (1)*University of California at Davis*, (2)*M.I.N.D. Institute, University of California at Davis*

Background: There is mounting evidence of an association between the presence maternal anti-fetal brain autoantibodies and development of autism in some children. Particularly, human fetal brain antigens of approximately 37kD and 73kD are detected by western blot in some mothers of children with autism. Observations suggest that the antigen(s) are relatively highly expressed in human as well as Rhesus macaque fetal brain. Characterization of the antigen distribution during fetal development, as well as in several mammalian cell lines of different origin, will help in identifying the target(s) of, and a potential role for, these antibodies.

Objectives: Determine the temporal distribution and abundance of the autoantigen(s) in fetal Rhesus monkey brain at several developmental time points. To help determine which cell types express the autoantigen(s), several mammalian cell lines were also assessed.

Methods: Plasma IgG antibodies from mothers of children with autism as well as mothers of typically developing children as matched controls. Samples from each group were used to stain western blots of fetal Rhesus macaque brain ranging from 49 to 152 days gestation. Protein extracts of neuronal and non-neuronal cell lines were similarly assessed for antigen expression by western blot.

Results: Expression of the specific fetal brain antigens recognized by maternal antibodies was present at low levels in early gestation (day 49) and peaked at 152 days. Furthermore, expression of these antigens was observed in two transformed neuronal cell lines, but absent in a fibroblast and breast cancer cell line.

Conclusions: We have demonstrated that the specific proteins recognized by maternal IgG from mothers of children with autism are expressed more abundantly later in fetal brain development. This suggests that the antigens recognized by these maternal antibodies may relate to higher order function due to their later temporal expression. The presence of the autoantigen in some cell lines will provide information as to the tissue specificity as well as an additional source of antigen for protein identification.

120.86 86 CD40L, a Marker of Systemic Inflammation Is Increased in Patients with Autism. C. A. Pardo*[1], H. Khan[1], L. C. Lee[2], S. J. Spence[3], A. Thurm[4] and S. E. Swedo[4], (1)*Johns Hopkins University School of Medicine*, (2)*Johns Hopkins Univ. School of Public Health*, (3)*NIH*, (4)*National Institute of Mental Health, National Institutes of Health*

Background:
Autism is a disorder determined by multiple interacting genetic and environmental factors in which immune responses and neuroinflammation appear to influence pathogenic mechanisms and persistence of neurological and behavioral abnormalities.

Objectives:
To identify biomarkers of systemic inflammation in patients with regressive (AUT-R) and non-regressive (AUT-NR) forms of autism.

Methods:
A case-control study of clinical and immunological factors associated with autism was carried out at the intramural autism program of the National Institute of Mental Health. Autism was diagnosed using the ADI-R and ADOS as well as clinical judgment. Regression history was also assessed using the Regression Validation Interview. Regression was defined as language loss and/or loss of social engagement. Serum and plasma samples were obtained from 46 patients with autism (25 AUT-R and 23 AUT-NR; mean age 4.14 years ±1.31) and age-matched typically developing controls (mean age 3.32 ± 1.28). Multiplexed flow cytometric bead assays were used to determine the profile of 27 cytokines, chemokines and growth factors in serum. The Mann-Whitney U-test was used to compare group differences in analyte concentrations. Statistical significance was determined at 0.05.

Results:
CD40 ligand (CD40L), also called CD154 or TNFSF5, was significantly elevated in cases of autism compared to controls (p 0.018). CD40L is a transmembrane glycoprotein related to tumor necrosis factor and is a strong inducer of Th1 cell responses and central to the maintenance and development of B and T cell responses, The chemokine eotaxin (CCL11) and the hematopoietic growth factor, Granulocyte-Macrophage colony stimulating factor (GM-CSF), were identified to be significantly decreased in the serum of patients with autism as compared with controls (p=0.017 and 0.004 respectively). Although the levels of expression of IL-10 and IL-5 were similar in the overall analysis of autism compared to typical control groups, these two cytokines did show significant decreases in the AUT-R patients as compared with typical controls (p 0.019 and 0.048).

Discussion

The elevated concentration of CD40L in serum of patients with autism supports the view that an underlying systemic inflammatory process occurs in patients with this disorder, a condition that may influence overall health, CNS function and behavior. CD40L increases in the serum of patients with autism may result from systemic inflammatory events that exists as co-morbid conditions or from an increase in oxidative stress pathology . CD40L may work as an amplifier of pro-inflammatory and immune responses in the CNS and be involved in processes of neuroglial activation. Reductions in subsets of cytokines such as IL-10, IL-5 and GM-CSF and chemokines such eotaxin, suggests that dysfunction in immune responses occurs in patients with autism.

Conclusions:

Evidence of activation of the CD40/CD40L pathway is an indicator of systemic inflammation in patients with autism that may be associated with overall effects on the health, neurological and behavioral status.

120.88 88 Is Lead a Concern in Autistic Children?. B. G. Clark* and I. Buka, *University of Alberta*

Background:

Lead is a known environmental toxin that affects the nervous system. Little research on prevalence of blood lead levels in developmentally affected children is available. Currently, there are no Canadian programs that offer surveillance of blood lead levels in young children or in "at risk" developmentally delayed groups although they are identified as being at risk for potential exposures. Although the Centre for Disease Control (CDC) and Health Canada report regulatory levels of lead as 10 ug/dL or 0.48mmol/L, new research suggests levels of greater than 2 µg/dL or 0.1 mmol/L may affect IQ and behavior in young children.

Objectives:

To compare the blood lead levels in a sample of autistic children living in Northern Alberta with standards provided by the CDC guidelines.

Methods:

Children with a diagnosis of Autism were recruited from the Preschool Assessment Service and Autism follow-up clinics at the Glenrose Rehabilitation Hospital in Edmonton, Alberta. A CBC & differential, ferritin and blood lead were requested after consent was obtained. Summary statistics were reported as means with standard deviation as well as medians with ranges. For dichotomous outcomes rates were presented.

Results:

Table 1: Summary of blood work findings of Autistic cohort

Outcome [Unit]	Number (n)	Mean (SD)	Median (Range)
Age [years]	48	5.4 (2.1)	5.0 (3.0-10.8)
Blood Lead [umol/L]	48	0.082 (0.082)	0.05 (0.02-0.42)
Hemoglobin [g/L]	42	130.94 (8.3)	131.5 (111-150)
MCV [fL]	42	82.2 (4.5)	83 (61-88)
Ferritin [ug/L]	40	29.8 (17.7)	25 (7-86)

None of the children had levels exceeding the current limits set by the CDC related to unsafe levels of blood lead. Nine (19%) had levels greater or equal to 0.1 umol/L but less than 0.48 umol/L. 39 children (81%) had blood levels less than 0.1 umol/L .

Conclusions:

Autistic children in Northern Alberta may not have a concern with elevated blood lead levels that exceed current CDC guidelines. Clinicians may need to explore the reasons for low level exposures to lead further and provide primary prevention for all children at risk.

120.89 89 Increasing Blood Draw Compliance in Children with ASD. E. Hanson, C. Davit* and R. Hundley, *Children's Hospital*

Background: An increasing number of studies are commencing to understand the genetic underpinnings of autism spectrum disorders

(ASD). In order to obtain the necessary data, most require a blood draw from the affected proband. In our current sample of 245 children who have completed the genetics appointment, 35 children were unable to complete the blood draw due to behavioral difficulty (15%). In order to address this significant issue, we have developed a protocol designed to increase comfort and compliance with blood draws. Social stories, picture schedules, and positive reinforcement have been shown to reduce anxiety and increase compliance to health care procedures among children with ASD (Ghuman et al., 2004). We decided to utilize all of these modes in our intervention.

Objectives:

1. Develop a novel intervention to increase compliance with venipuncture for children with ASD.
2. Evaluate the success rate of the intervention once entered into the training.
3. Describe children's and parents reaction to the intervention.
4. Describe which factors in the intervention were most helpful for achieving a successful blood draw.

Methods:

Since initiating our intervention program, 34 families have been screened for study participation. Of these families, 13 have requested to participate (38%). We have completed the intervention thus far with 2 of these families. We anticipate completing the intervention and data collection by the IMFAR meeting.

We followed the guidelines established by Gray and Garand (1993) to create individualized social stories for each child. The stories detail the multi-step process of having ones blood drawn, broken down into five distinct practice sessions. Each completed practice session ends with a positive reinforcement (reward) for the child. The reward is chosen for its salience for each individual child.

Additionally, each child receives an individualized Boardmaker picture schedule outlining the venipuncture procedure. This includes a side-by-side comparison of how compliance during the procedure leads to a reward, while negative behaviors will not end in reward

Accompanying the social stories and picture schedule is a kit of venipuncture materials for the children to use as part of the practice session, including rubber gloves, alcohol swabs, band-aids, an elastic tourniquet, and a 5ml plastic syringe. Each session begins with the child gradually experiencing a new venipuncture-related material (i.e. putting on gloves, tying the tourniquet) culminating with administration of a pretend shot. The parents are encouraged to practice for 1-2 weeks before the blood draw.

After the blood draw session, families receive an internet-based or hard copy general satisfaction survey. We inquire about the length and duration which they practiced, as well as which aspects were most useful.

Results:

In our first 2 children with ASD, both were able to complete the blood draw successfully. Researcher report has described probands repeating the language learned through the social story, to reaffirm the actual venipuncture is just as practiced.

Conclusions:

Our preliminary findings have shown a high interest and two successes to date. Positive response to our intervention has important implications for venipuncture for children with ASD in both clinical and research settings.

120.90 90 Measuring the Effects of Therapeutic Horseback Riding in Children with Autism Spectrum Disorders. R. Gabriels*[1], J. A. Agnew[1], G. H. Clayton[1], Z. Pan[1], K. Holt[1], S. Ruzzano[1], H. Bosler[1], R. Howard[1] and G. Mesibov[2], (1)*The Children's Hospital/University of Colorado Health Sciences Center*, (2)*University of North Carolina at Chapel Hill*

Background: **Background:** Therapeutic horseback riding (THR) has been used to enhance functioning in many individuals with disabilities in Canada and the U.S. for over 40 years, but there are few studies to guide consumers. Children diagnosed with an autism spectrum disorder (ASD) have social, communication, behavior, emotional, and dependency issues and caregivers struggle to find helpful interventions for these children.

Objectives: Evaluate effects of ten weekly one-hour lessons of a standardized THR treatment approach on three core areas: 1) self-regulation behaviors, 2) adaptive daily living skills, and 3) motor coordination, organization and planning.

Methods: Thirteen children with an ASD received pre- and post-evaluations including the Aberrant Behavior Checklist - Community (ABC-C), Vineland Adaptive Behavior Scales-II (VABS-II), Bruininks-Oseretsky Test of Motor Proficiency (BOT-II), and Sensory Integration and Praxis Test (SIPT) within one month prior to and following engagement in 10 weeks of THR lessons. Caregivers and THR therapists completed ratings (ABC-C) of the child's behaviors on a weekly basis.

Results: For this abstract, pre/post intervention changes were available for 13 participants. All assessments were evaluated by two-tailed t-test with a test of significance set at an alpha of 0.05. Mean age upon enrollment of this group of patients (n=13) was 10.1±3.2 years. The group had an average Leiter IQ of 91.3±22.7. Post intervention changes in VABS-II subscale scores were significant for the Adaptive Total Score ($p=0.01$) and trended towards significance (i.e. $0.05 < p < 0.1$) for the Communication raw scores and Daily Living raw scores. BOT-II short form scores demonstrated a significant improvement ($p=0.02$). Improvements in SIPT verbal praxis scores were noted to be significant ($p=0.003$) whereas changes in postural praxis scores were not significant. When rated by parents, changes in ABC-C subscale scores for Irritability, Hyperactivity, Lethargy and Stereotypy were found to be significant, but changes in the Inappropriate Speech subscale were not significant. When evaluated by the THR trainer, no significant changes were evident in any of the ABC subscales.

Conclusions: The preliminary data analyses presented above suggest that participation in a well-defined Therapeutic Horseback Riding program of 10 weeks duration can demonstrate a significant improvement in several behavioral and physical parameters. Measures of behavior, adaptive living skills and motor coordination and planning improved statistically over the course of THR. The study is ongoing and additional data will be obtained to corroborate significant changes noted for this group and validate or disprove noted trends. Future work is planned to address additional questions such as length of effect and specificity of therapy.

120.91 91 Reduction in Salivary Cortisol Following Physical Exercise and Relaxation among Adolescents and Young Adults on the Autism Spectrum. A. Hillier* and D. Murphy, *University of Massachusetts Lowell*

Background: High levels of stress and anxiety are frequently seen among those with autism spectrum disorders (ASD). Past research has demonstrated that physical exercise, relaxation, and physical health are all positively associated with well-being. However, little research has focused specifically on the young adult autism population, and there has been minimal utilization of objective measures of stress.

Objectives: We implemented an 8-week physical exercise and relaxation intervention for adolescents and young adults on the autism spectrum which aimed to reduce levels of stress and anxiety.

Methods: Levels of salivary cortisol (a stress hormone) were compared before and after half of the sessions. A self-report measure of anxiety was also implemented. In addition, reports of stress were assessed pre and post the 8-week program.

Results: Cortisol levels showed a significant reduction at the end of the sessions compared to levels at the beginning. These findings were supported by the self-report measure of anxiety. Measures completed pre and post the 8-week program also showed a reduction in self-reported stress following participation in the program.

Conclusions: Our findings highlight the effectiveness of exercise and relaxation for improving symptoms of anxiety and stress among those with ASD. Greater emphasis is needed on assessing the utility of similar non-pharmacological interventions.

120.92 92 Adolescents with Asperger's Syndrome Impaired in Several Domains of Executive Function as Measured by the Behavior Rating Inventory of Executive Function. T. Oswald*, M. A. Winter-Messiers and L. Moses, *University of Oregon*

Background:

There are inconsistent results in the literature about executive dysfunctions in individuals with higher functioning forms of autism, specifically in planning, set-shifting, and working memory (Ozonoff, South, & Miller, 2000; Goldberg, Mostofsky, Cutting, Denckla, & Landa, 2005; Ozonoff & Strayer, 2001). Gioia et al. (2002) examined executive functions in children with higher functioning forms of autism; Asperger's

Syndrome, PDD NOS, and higher functioning autism (HFA). They used the Behavior Rating Inventory of Executive Function (BRIEF), a parent report measure of executive function. The study found that these children were significantly elevated across all scales relative to controls. These data suggest that the children with higher functioning ASD are impaired in planning/organization, shifting, working memory, emotional control, initiation, monitoring and organization of materials. Further, these results indicate that parent reports of executive function, as measured by the BRIEF, may be an important tool for illuminating our understanding of the executive dysfunctions present in higher functioning forms of autism. Currently, there is a lack of BRIEF data on adolescents with higher functioning forms of autism. Yet, executive functions greatly develop during adolescence in the typically developing population and so studying this developmental stage is critically important for characterizing atypical development of executive functions in individuals with higher functioning forms of autism.

Objectives:

The objective of the current study was to examine whether adolescents with Asperger's Syndrome compared to matched typically developing controls are reported to have impairments in executive functions across the 8 scales of the BRIEF.

Methods:

The current study examined executive functioning in 17 adolescents with Asperger's Syndrome (8 Female; 9 Male) and 17 typically developing adolescents matched for gender and age and less closely matched for IQ. One parent, typically mothers, of each of the thirty-four children, filled out the BRIEF.

Results:

Parents reported that adolescents with Asperger's Syndrome had significantly poorer executive function abilities than typically developing controls across all of the scales of the BRIEF (see Table 1), except for the Organization of Materials scale which was approaching significance.

Table 1.

Paired Samples T Tests for BRIEF Scales

Subscale	t-test (df =16)	p value
Inhibit	-4.43	**
Shift	-7.58	**
Emotional Control	-4.83	**
Initiate	-7.45	**
Working Memory	-9.11	**
Plan/Organize	-10.78	**
Monitor	-4.43	**
Organization of Materials	-1.72	0.11

** = p < .001

Conclusions:

The current study suggests that adolescents with Asperger's Syndrome have impairments in several domains of executive function, specifically in planning/organization, shifting, working memory, emotional control, initiation, and monitoring. Furthermore, the results suggest that the BRIEF may be used in the future as an important instrument to help reveal the nature of executive dysfunctions in adolescents with higher functioning forms of autism.

120.93 93 Autistic Traits and Sociometric Assessment: a Pilot Study. M. O. Mazurek*[1] and S. M. Kanne[2], (1)*Thompson Center for Autism and Neurodevelopmental Disorders*, (2)*University of Missouri*

Background: Although autism spectrum disorders (ASD) are associated with marked social

impairment, almost no empirical research has been devoted to understanding the actual impact of ASD symptoms on children's social standing within naturally-occurring peer groups. This knowledge is important for identifying the symptoms that are most salient and problematic in the peer group, both for designing interventions and for evaluating treatment outcome.

Objectives: The purpose of this pilot study was to provide a first look at the use of sociometric methodology in obtaining direct information from peers regarding the social impact of autistic traits.

Methods: The sample included 19 school-aged children enrolled in an after-school program. Sociometric assessment was conducted with each child and autistic traits were assessed using the Social Responsiveness Scale.

Results: We found significant associations between overall symptoms of ASD and both social acceptance and social visibility. As expected, we found that higher levels of autistic traits are associated with greater peer dislike. The results also demonstrated that specific types of symptoms are associated with more negative effects in the peer group.

Conclusions: Sociometric assessment appears to be a feasible and informative approach for examining the impact of autistic traits on real-world peer relations. These results have implications for both treatment and future studies.

120.94 94 Social Responsiveness Scale: Standardization and Validation of the Dutch Adult Version. W. De la Marche*[1], J. Steyaert[1], E. M. Scholte[2], M. H. Dorst[3], I. A. van Berckelaer-Onnes[2] and I. L. J. Noens[4], (1)*UPC-K.U.Leuven*, (2)*Leiden University*, (3)*Universiteit Leiden*, (4)*Katholieke Universiteit Leuven*

Background:

Autistic traits tend to be continuously distributed in the general population (Constantino & Todd, 2003; Ronald et al., 2006). The Social Responsiveness Scale (SRS) (Constantino et al., 2003) is a 65-item reporter based questionnaire with a total score and 5 theory-based subscales. This informant-report questionnaire has proven to quantify autistic traits in a reliable way. We translated the adult research SRS into Dutch and generated a self-report version for adults of this questionnaire. Both versions were back translated into English and approved by Dr. Constantino and the original publisher.

Objectives:

1) To confirm the validity of the Dutch informant-report SRS in the general Dutch-speaking population (Netherlands and Flanders (Belgium)).
2) To validate the Dutch self-report questionnaire in the same population.
3) To describe the distribution of autistic traits as measured by the SRS in the general population.

Methods:

Randomly selected adults in Flanders and the Netherlands are asked by e-mail to participate. They can register on an internet website and fill out SRS questionnaires about themselves and their partner, and their partner is asked to do the same. Only questionnaires without missing items are taken into account for the analyses. We will produce descriptive statistics (distribution of SRS-scores in the general population, for both men and women) and measures of reliability (test-retest, interrater, internal consistency of total scores and subscale scores) of both versions of the Dutch SRS. A factor analysis will be carried out on the other-report as well as the self-report questionnaire.

Results:

Preliminary results from the Netherlands (N=538 for self-report, N=370 for partner-report) show a good (two week) test-retest reliability (self-report: 0.86 for total score, 0.65-0.84 for subscale scores; partner-report: 0.82 for total score, 0.64-0.85 for subscale scores). Total internal consistency is high for both versions of the Dutch SRS (0.92 for self-report, 0.95 for other-report), with two items not (or even negatively) correlating with the total score. Subscale internal consistencies are sufficiently high as well (0.56-0.83 for self-report; 0.67-0.89 for partner-report). More results will be available at the IMFAR conference.

Conclusions:

The preliminary results suggest that the Dutch Social Responsiveness Scale for Adults and the newly developed self-report version of this questionnaire have psychometric properties comparable to the original questionnaire.

120.95 95 Adaptive Behavior and Cognitive Skills for Young Children on the Autism Spectrum: An Examination of the Updated Vineland-II and Bayley-III. C. E. Ray-Subramanian*[1], N. Huai[1], S. Ellis-Weismer[2] and M. A. Gernsbacher[2], (1)*Waisman Center, University of Wisconsin-Madison*, (2)*University of Wisconsin-Madison*

Background: Assessment of adaptive behavior is a key component of a comprehensive diagnostic evaluation for individuals on the autism spectrum, individuals with intellectual disabilities, or individuals with other developmental disabilities. For the second edition of the Vineland Adaptive Behavior Scales (Vineland-II) published in 2005, revisions and additions were included to better measure adaptive skills in very young children and to capture qualitative differences in communication and social interaction for individuals on the autism spectrum (Sparrow, Cicchetti, & Balla, 2005). However, published research to date examining adaptive behavior in individuals on the autism spectrum has been based largely on the original 1984 version of the Vineland Adaptive Behavior Scales. Furthermore, existing research has not examined the relation between the Vineland-II scales and the Cognitive scale of the Bayley Scales of Infant and Toddler Development-Third Edition (Bayley-III) for young children on the autism spectrum. The current study investigated adaptive and cognitive skills for a sample of young children on the autism spectrum using the Vineland-II and Bayley-III.

Objectives: This study analyzed the adaptive behavior profile of a sample of two-year-old children on the autism spectrum using the Vineland-II. In addition, correlations between the participants' Bayley-III Cognitive developmental ages and Vineland-II subscale age equivalent scores were examined.

Methods: Participants were 112 children (mean age = 31 months) diagnosed as being on the autism spectrum who were part of a longitudinal study of early language development. Autism spectrum diagnoses were determined using comprehensive diagnostic evaluations that included the ADI-R and ADOS. The Vineland-II Survey Interview Form and the Bayley-III Cognitive scale were administered as part of the participants' initial evaluation.

Results: A general pattern of adaptive behavior emerged with statistically significant differences between each of the four mean domain standard scores (t ranged from 3.71 to 13.54; df = 111 and $p<.000$ for all tests): Motor Skills (mean SS = 88) was the highest, followed by Daily Living Skills (mean SS = 80), Socialization (mean SS = 77), and Communication (mean SS = 74). Bayley-III Cognitive developmental ages were significantly correlated with age equivalent scores for each of the Vineland-II subscales: Receptive Communication (r = .62), Expressive Communication (r = .62), Personal Skills (r = .54), Domestic Skills (r = .42), Community Skills (r = .51), Interpersonal Relationships (r = .53), Play and Leisure Time (r = .38), Coping Skills (r = .41), Gross Motor Skills (r = .37), and Fine Motor Skills (r = .58).

Conclusions: Although it is not a diagnostic tool for identifying individuals on the autism spectrum, the Vineland-II identified patterns reflecting qualitative weaknesses in communication and social interaction for children on the autism spectrum as young as two years of age. In contrast with previous research demonstrating weak relations between Wechsler scales and the Vineland-II for older, typically developing children and adolescents (e.g., Sparrow, Cicchetti, & Balla, 2005), the current study found significant correlations between Bayley-III Cognitive developmental ages and age equivalents on each of the Vineland-II subscales for two-year-old children on the autism spectrum.

120.96 96 The Broader Autism Phenotype in Italy. A Research Study Using the Autism-Spectrum Quotient - Italian Version. L. Ruta*[1], L. Mazzone[1], N. Russo[1], V. Mannino[1], S. J. Wheelwright[2] and S. Baron-Cohen[2], (1)*University of Catania, Italy*, (2)*University of Cambridge*

Background: The Autism-spectrum Quotient (AQ) is a brief, self-administered instrument for quantifying the number of autistic traits in adults with normal intelligence.
In particular, the AQ measures where a person lies on a continuum of social-communication disability, in clinical samples and the general population.
The instrument demonstrates high reliability and remarkable cross-cultural stability in both Japanese and British culture, with the Japanese AQ mean scores higher than the British.
Objectives: To investigate the distribution of autistic traits and the broader autism phenotype

(BAP) in a sample of Italian parents of typically developing children and parents of children affected by Autism Spectrum Condition (ASC).
Methods: A group of 545 participants matched for age, including the parents of children with ASC (115 fathers and 130 mothers) and typically developing children (150 fathers and 150 mothers) filled out the Italian version of the AQ. The Italian AQ was translated using a back translation procedure. The questionnaire was completed during outpatient visits at Catania University Hospital in the ASC group. The control group (CG) was recruited from three large public mainstream schools in the city centre and the province of Catania, attended by multicultural pupils and the questionnaires were sent out by mail or email to the CG parents.
Results: A main effect of group and sex was demonstrated for the total AQ and the subscales of Social Skill, Communication and Imagination, with ASC parents scoring significantly higher than CG parents. In particular, ASC fathers scored the highest, ASC mothers scored similar to CG fathers and CG mothers scored the lowest. Finally, males scored significantly higher than females.
Conclusions: Our results suggest that despite being tested in a culturally different population (Italy), ASC parents displayed more autistic traits than parents of typically developing children. This confirms the liability for autism expressed by non-autistic relatives, in a phenotype that is milder but qualitatively similar to the defining features of autism (BAP). This study also replicates the finding that males report more autistic traits compared to females, in line with the "Extreme Male Brain Theory" of autism.

120.97 97 Sensory Sensitivities and the Autism Spectrum Quotient.

A. E. Robertson* and D. R. Simmons, *University of Glasgow*

Background:

There is a variety of evidence which suggests that individuals with ASD show atypical responses to sensory stimuli. Is there a correlation between the degree to which ASD-like traits are displayed in an individual and the level of atypical sensory responses experienced?

Objectives:

- To construct a sensory questionnaire that could be self-administered by individuals with ASD (as well as typical participants) to give an informative "sensory score".
- To determine whether there was a correlation between AQ score (i.e. performance in the Autism Spectrum Quotient questionnaire of Baron-Cohen et al, 2001) and sensory score in our sample.
- To find out which situations/sensory stimuli/environments people with a high AQ score found problematic.

Methods:

A sensory questionnaire was developed and posted on a publicly accessible website. This sensory questionnaire consisted of 75 items (70 closed, 5 open). Closed questions were distributed equally between 7 modalities (visual, auditory, tactile, gustatory, olfactory, vestibular and proprioceptive) and investigated both "hyper" and "hypo" aspects of each modality. The total sensory score was calculated based on the number and severity of the reported sensory symptoms. The AQ was administered alongside the sensory questionnaire. The web-site address was publicized within the university, via personal contacts of the authors and an online forum for people with ASD.

Results:

There were 176 responses (68.2% female; 31.8% male), with AQ scores ranging between 5 and 49. A significant linear correlation was observed between the AQ scores and the total sensory scores ($r = 0.772$, $p < .0001$). Of particular interest was the discovery that mid-section AQ scorers (i.e. those who may have some traits of ASD but unlikely to be diagnosed as having AS/HFA [18<AQ<32]) had significantly higher sensory scores than individuals with a more 'typical' score [i.e. AQ < 19] [$t(138) = 8.1$, $p < .0001$]. This relationship held when the sensory scores were separated into responses to hyper questions and those to hypo questions. Content Analysis was used for the open questions. Many individuals with high AQ scores found particular sensory stimuli to be problematic, e.g. cluttered visual environments, loud noises and strong odours.

Conclusions:

1. There was a strong positive correlation between AQ score and sensory score in our sample.

2. Middle-scorers in the AQ had a significantly higher sensory score than the low-scorers, and a significantly lower score than the high-scorers.

3. Problematic environments mentioned by those with a high AQ score were varied, but supermarkets and strong-smelling shops (e.g. perfume shops) were indicated frequently. Some people said that they could not physically enter such environments, and therefore resorted to using the internet to do their shopping.

4. In our sample, individuals with high AQ scores indicated in their responses to the open questions that, despite being motivated to interact socially, it was often too difficult or painful due to the aversive nature of the sensory environment.

5. These data suggest that atypical sensory responses may play a role in increased social isolation.

References:

Baron-Cohen et al. (2001). *J. Aut. Dev. Dis., 31,* 5-17.

120.98 98 The Hebrew Version of the Autism Spectrum Quotient (AQ-Heb) as a Screening Instrument for Adults with Autism Spectrum Conditions. O. Golan*, R. Gold and S. Fridenzon, *Bar-Ilan University*

Background: The broader definition of Autism Spectrum Conditions (ASC) resulted in diagnosis of individuals with ASC way into adulthood. This called for screening instruments which could assist in defining the need for a full clinical diagnosis amongst adults, especially in countries in which diagnosis of Asperger Syndrome (AS) and High Functioning Autism (HFA) has not been common. This study evaluates The Autism Spectrum Quotient (AQ, Baron-Cohen et al, 2001), in its Hebrew version (AQ-Heb), as a self-report instrument for adults, screened for ASC in Israel.

Objectives: To evaluate the statistical properties of the AQ-Heb with a sample of adults diagnosed with ASC and a matched sample of adults from the general population. In addition, we compared a self vs. parental report on the AQ for a subsample of the two groups.

Methods: The clinical group comprised 41 adults (11 females), diagnosed with ASC by professional clinicians according to DSM-IV criteria. They were matched to a general population group of 123 adults (44 females) on age, sex ratio, and level of education. Participants in both groups filled in the AQ-Heb. In the second part of the study, parents of 20 adults from each group filled in the AQ-Heb with regards to their children.

Results: the clinical group scored significantly higher on the ASC-Heb, compared to the general population group, with no sex differences in either group. The average AQ-Heb score for the clinical group (Mean=27.2, Std.=8.0) was lower than previously reported. A cutoff score of 22 yielded sensitivity of 0.73 and specificity of 0.82. In addition, a significant correlation between age and AQ-Heb score (r=0.32) was found only for the clinical group. Parental reports on the AQ-Heb were significantly higher than self-report for the clinical subsample, but not for the general population subsample. These findings may reflect poor self-awareness amongst some of the young adults diagnosed with ASC. Similar findings have been previously reported with British participants (Golan & Baron-Cohen, 2006).

Conclusions: The AQ-Heb may serve as a good screening instrument for ASC amongst Israeli adults. However, in scores close to the cut-off, especially with younger respondents, additional parental report may be required as part of the screening process.

120.99 99 Psychiatric Comorbidities in Patients with Asperger Syndrome and High Functioning Autism: Clinical and Treatment Implications. M. C. Porfirio, G. Giana*, B. Manzi, S. Benedetti, A. Benvenuto, F. Caretto and P. Curatolo, *Tor Vergata University*

Background: Psychiatric disorders are common and frequently multiple in children with autism spectrum disorders (ASD), but only few systematic and structured studies have investigated the psychiatric comorbidities in ASD. Furthermore, changes in mood and behavior are wrongly attributed to the individual's developmental disorder rather than to a comorbid psychiatric condition.

Objectives: This study evaluated retrospectively the psychiatric comorbidities in patients with High Functioning Autism/ Asperger Syndrome (HFA/AS), referred to the Child Psychiatric Department of "Tor Vergata" University in the period 2003-2008.

Methods: Participants were 79 children, adolescents and young adults (73 males, 6 females), aged between 4-30 years and all had a QI over 65 on Weschler Scale. Subjects were assessed for both ASD and psychiatric disorder by an experienced child psychiatrist utilizing ADI-R, ADOS and DSM-IV psychiatric diagnostic assessment (K-SADS, CBCL, CDI, MASC, Conner's Scales and SNAP-IV).

Results: The rate of psychiatric disorders in this group was 55%. Attention Deficit Hyperactivity Disorder (ADHD) was the most frequent associated psychiatric condition, observed in 28/79 patients (35%). Many children with HFA/AS often were initially misdiagnosed with ADHD. Bipolar spectrum disorders were observed in 5/79 patients (6%). Other comorbidities included anxiety, tics, obsessive symptoms, oppositional defiant and conduct disorder. 20 of 79 (25%) patients received a pharmacological treatment for comorbidities, that led a decrease in problematic behaviors and improve clinical functioning.

Conclusions: This study shows a very high rate of psychiatric disorders in this group and suggest that diagnosis of an ASD should be routinely followed by systematic assessment for other psychiatric disorders. Detecting psychiatric comorbidities may help to identify targets for specific intervention that could reduce overall impairment and improve quality of life.

120.100 100 A Comparison of Maternal and Paternal BASC Scores for Individuals with ASD. M. Hale, H. Bryant*, A. Beaumont, J. Durocher, A. Gutierrez and M. Alessandri, *University of Miami*

Background: Previous research has generally indicated that maternal and paternal reports of childhood behavioral functioning, as measured by the Behavior Assessment System for Children (BASC) (first and second editions) are often inconsistent. Some research suggests that fathers underreport symptoms relative to the mother report, while others suggest that mothers and fathers are each sensitive to specific types of symptoms thus making their reports dissimilar. Previous research has primarily focused on various childhood disorders and typically developing children, but there is very little research investigating differences in parental reports of behavioral functioning from parents of children with Autism Spectrum Disorders (ASDs).

Objectives: To explore the possible differences between maternal and paternal reports on the BASC for children with an ASD. Furthermore, to determine whether there are specific differences between maternal and paternal reports on the BASC within diagnosis (Autistic Disorder, Asperger's Disorder, and PDD-NOS).

Methods: Methods included a retrospective chart review of 40 files from the Autism Spectrum Assessment Clinic at the University of Miami. Reviewed charts included children and adolescents who were diagnosed with an ASD, and whose chart included BASCs completed by both mother and father. The sample includes: 10 PDD-NOS, 9 Asperger's Disorder, and 21 Autistic Disorder. Data pertinent to the study were extracted including maternal and paternal reports on either the BASC 1 or BASC 2.

Results: Paired sample t-tests indicated no significant differences between maternal and paternal reports when all children with ASD were included in the analysis, and within the PDD-NOS group. Analysis for children in the Asperger's Disorder revealed that mothers' ratings were significantly higher than fathers' in the Attention Problems domain, and, in the Autistic Disorder group, mothers' ratings were significantly lower in the areas of Daily Living Skills, and Adaptive Skills.

Conclusions: Analyses suggest that in general, maternal and paternal ratings of children and adolescents with ASD on the BASC are very similar, while within each diagnosis there are some differences where, in general, mothers report more impairment. Implications of these findings suggest that clinicians should be aware of the potential similarities and differences in reporting patterns between parents, and should utilize that knowledge when making diagnostic or behavioral conclusions and recommendations.

120.101 101 Personality Disorder Assessment in the Differential Diagnosis of Autism Spectrum Disorders in Adults. C. H. Morton*, A. C. Ruocco, M. A. Shanahan, M. Voss and L. D. Stanford, *University of Illinois at Chicago*

Background: Given the common features of rigidity of thinking, persistence and pervasiveness of symptoms, and the negative impact on one's functioning, the differential diagnosis between an Autism Spectrum Disorder (ASD) and a Personality Disorder (PD) in adults can be difficult. Many of the characteristic features of ASD resemble traits associated with specific personality disorders, particularly the odd or eccentric Cluster

A PD's, and inadequate characterization of personality and neurodevelopmental disorders in adults referred for a diagnostic evaluation could lead to misdiagnosis. However, the use of PD instruments in the assessment of adults with ASD's is relatively uncommon and vice versa. Personality assessment in combination with the Autism Diagnostic observation Schedule (ADOS) can provide a more comprehensive characterization of the interpersonal and emotional difficulties experienced by these adults and improve specificity of diagnosis.
Objectives: We present the case of MR, a 42-year old male who was referred by his treating psychiatrist for evaluation of possible ASD, such as Asperger's Disorder. MR has a history of depression, persistent social isolation, and pervasive anxiety as well as academic and employment difficulties. Previous diagnoses have included Schizoaffective Disorder, Major Depressive Disorder, Paranoid Schizophrenia, and anxiety. Additionally, symptoms of grandiosity and odd thinking were observed.
Methods: MR was administered a comprehensive battery of neuropsychological and behavioral instruments that included measures of intelligence, academic achievement, visuospatial processing, and fine motor functioning as well as a questionnaire specific to symptoms of inattention. In addition, MR was administered Module 4 of the ADOS, the Structured Interview for DSM-IV Personality (SID-P), and a self-report measure of personality.
Results: MR met criteria for Autistic Disorder based upon the ADOS. In addition, he met criteria for Narcissistic PD and was one symptom below criteria for five other PD's. MR also demonstrated bilateral fine motor deficits. Otherwise, his neurocognitive abilities were well-developed.
Conclusions: MR's symptom profile and test performance were most consistent with Autistic Disorder. However, conclusions were limited based upon his refusal to allow the examiner to contact family members in order to confirm age of symptom onset, and the diagnosis of Autism was made provisionally pending substantiation of developmental history. Although MR exhibited characteristics of several personality disorders, particularly Narcissistic Personality Disorder, these traits existed within the context of Autism rather than a PD. Specifically, his symptoms were primarily related to a lack of insight regarding social relationships rather than a wanton disregard for the feelings of others.

120.102 102 Differential Diagnosis of ASD Subtypes and ASD v. Nonspectrum Disorders in a Clinic-Referred Sample: Application of Two Diagnostic Approaches. A. N. Esler* and R. K. Rumsey, *University of Minnesota*

Background: Diagnostic distinction among autism spectrum disorders (ASD) has been a topic of considerable debate, with some clinicians and researchers questioning the validity of distinctions across subtypes. While clinicians, both experienced and inexperienced, generally make reliable diagnostic distinctions between cases of Autism versus non-ASD, interrater reliability decreases significantly for Autism v. nonautistic ASD (Klin et al., 2000), particularly for inexperienced clinicians. Application of DSM-IV criteria improved interrater reliability for inexperienced clinicians. Inconsistent and varying diagnostic schemes used by different researchers further complicate the debate (Volkmar & Klin, 2000), and there are criticisms regarding the shortcomings of current DSM-IV/ICD-10 definitions. Researchers have questioned the validity of giving Autistic Disorder priority over Asperger Syndrome (AS) in making diagnoses. Researchers at Yale developed a new set of criteria for AS based on specific behavioral features, without precedence given to Autistic Disorder. Using a sample selected to have a very high probability of having higher functioning autism (HFA) or AS, they found assignment of AS, HFA, and PDD-NOS varied greatly across three diagnostic systems (DSM-IV, presence of language delay, and the New System). Application of the New System resulted in more valid diagnostic distinctions between HFA, AS, and PDD-NOS (Klin et al., 2005). Interrater agreement for the New System was not calculated, as diagnoses were determined through consensus. Differentiating milder PDD-NOS from non-ASD disorders also proves difficult. In a study of DSM-IV/ICD-10 criteria, only a limited number of items differentiated PDD-NOS from non-ASD disorders (Buitelaar et al., 1999). Anecdotally, many clinicians with expertise in ASD report that they see many children who have been misdiagnosed ASD by other, less-experienced clinicians. In the ASD clinic from which the current sample is taken, close to 50% of children with previous ASD diagnoses were determined not to have ASD by the evaluation team.
Objectives: To examine interrater agreement using three diagnostic systems for diagnosis of HFA, AS, PDD-NOS, and nonspectrum in a clinic-referred sample.

Methods: Clinical records from 25 children referred to an ASD clinic for diagnostic evaluation were reviewed independently by two psychologists experienced in ASD, blind to diagnosis. Inclusion criteria were VIQ and NVIQ ≥ 70 and the following measures administered during evaluation: ADOS, SCQ, BASC-2, and a checklist of developmental history including age of first concern, first words, and first phrases.
Results: Results will be reported on interrater agreement on case assignment using strict DSM-IV criteria, and then again applying Yale's New System for AS. Data will be presented on Percent of Observed Agreement (PO) on diagnosis. Ratings of clinician level of confidence in diagnosis also will be presented and compared across diagnostic systems.
Conclusions: Consistency in defining and applying diagnostic systems for ASD and ASD subtypes is critical for replication and cross-site collaboration. This study provides evidence for validation of standard criteria for differential diagnosis of ASD, within ASD subgroups and between ASD and non-ASD disorders. Whereas past research selected samples based on high-probability of HFA or AS, this study provides support for application of standard criteria to a less straightforward, clinic-referred sample.

120.103 103 Autism and Anxiety: Incorporating Self Reports in Evaluating Whether Anxiety Is Elevated in Children and Adolescents with Autism Spectrum Conditions. K. D. Oden*[1], M. K. Vendlinski[1], B. A. Vlach[1], M. A. Gernsbacher[2] and H. H. Goldsmith[2], (1)*The University of Wisconsin-Madison*, (2)*University of Wisconsin-Madison*

Background: Only recently has the co-occurrence of autism spectrum conditions (ASC) with behavioral symptoms become a focus of research (Matson & Nebel-Schwalm, 2005). Individuals with ASC diagnoses are often expected to be at elevated risk for depression and anxiety (Howlin, 2000), although studies often lack adequate controls, use small or non-systematically obtained samples, and ignore ASC individuals' self-reports. Given that typically developing children as young as 3½ years can provide reliable reports of self-perceptions (Measelle et al, 2005), ASC individuals' self-reports deserve evaluation. Objectives: We evaluated the reliability and validity of ASC children's self-reports of anxiety and depression. Then, we investigated the association of ASC with anxiety and depression in children using multiple sources of information and multiple control groups. Methods: The main sample consisted of 112 children (all twins). For these analyses, inclusion in the ASC group required above-threshold scores on the SCQ or the ADOS. We administered the Berkeley Puppet Interview (BPI) to children and a companion instrument, the Health and Behavior Questionnaire (HBQ), to primary care providers. Research staff, blind to the child's ASC status, rated each child on a general anxiety scale. We also administered the BPI and the HBQ to a comparison group of twins, matched on cognitive ability, age, gender, and parental income. Results: ASC children provided reliable BPI self-reports, with Cronbach's alpha for the anxiety and depression scales exceeding .70. Evidence for validity came from significant correlations between corresponding HBQ and BPI subscales (e.g., depression, $r=.28$, $p<.05$; separation anxiety, $r=.37$, $p<.01$). The observer anxiety scale correlated more highly with the child BPI reports on the overanxious subscale ($r=.43$, $p<.01$) than with parent reports on the HBQ overanxious subscale ($r=.31$, $p<.05$). The correlations among the parent, child, and observer reports were not significantly different between the ASC and comparison groups. In the ASC versus non-ASC cotwin (i.e., discordant pair) comparisons (N=24 pairs), ASC twins reported slightly more depressive and anxious symptoms than their cotwins; however, these differences ($ds<=30$) were not significant. The parent reports did not indicate significant differences in depressive symptoms or separation anxiety, but did report higher overanxious symptoms in the ASC cotwins ($d = .59$, $p < .05$). The blind observer ratings of anxiety showed the smallest ASC versus non-ASC difference, with a non-significant difference of $d=21$. The ASC group's self-reports of depressive, separation anxiety, and overanxious symptoms were not significantly different from their matched comparison group (N=48, all non-ASC). In fact, the most deviant group appeared to be the non-ASC cotwins of ASC individuals, who self-reported less separation anxiety and less depression than their matched comparison group. Conclusions: Including the often-ignored perspective of ASC children in research appears justified. ASC children may exhibit slightly more anxious and depressive symptoms than their non-ASC cotwins, but the difference is small compared with matched comparison groups. Parents may over-report anxious and depressive symptoms in their ASC children, and non-ASC cotwins may under-report such symptoms.

120.104 104 Differential Diagnosis and Comorbidity of Autism and Schizophrenia Spectrum Disorders. J. Gorski*, R. Loftin and M. Huerta, *University of Illinois at Chicago*

Background: Although research supports the distinction between ASDs and child onset schizophrenia and other psychotic disorders (Konstantareas & Hewitt, 2001), the differential diagnosis of these disorders, in clinical practice, is often less obvious. Symptom overlap exists in the social domain, including limited affective expression,, narrow interests (White, Anjum, & Schulz, 2006), and lack of interest in friendships (Rappoport, 2001). In one study, over 88% of participants with Psychosis-NOS had a history of atypical social development (Nicoloson et al., 2001). Additionally, children in both groups demonstrate cognitive impairments, such as deficits in executive functioning, working memory, and attention (Lencz et al., 2006; Tsatsanis, 2005). As an increasing number of individuals with adequate language and cognitive function are identified with ASDs, the ability to distinguish psychosis from ASD symptommatology, and an understanding of how the two disorders may co-occur, is even more important.

Objectives: The current project expands on the existing findings from the research literature and qualitatively describes three cases which involved the differential diagnosis of ASD and psychosis (Autistic Disorder, Psychotic Disorder, NOS, and co-morbid ASD and Delusional Disorder). The authors will discuss themes illustrated by each case in relation to the existing literautre in order to inform the audience, as well as stimulate a discussion, about themes that emerge.

Methods: Each case received a comprehensive evaluation in a developmental disorders clinic which included assessment of cognition, adaptive functioning, developmental history (The Autism Diagnostic Interview- Revised) and child social-communication presentation (The Autism Diagnostic Observation Schedule). Social profiles are examined to highlight diagnostic differences between these disorders. In the context of case studies, particular attention is given to areas where symptoms appear to overlap including unusual social behaviors, such as suspicion and hostile attributions about the behavior of others; atypical language, such as use of stereotyped speech and reports of hallucinations; and circumscribed interests, which may be so all-consuming that they appear like delusions.

Results: Case studies will illustrate the ways in which differences between ASD and psychosis are evaluated, and clinical recommendations will be offered.

Conclusions: The differential diagnosis and comorbidity of autism and schizophrenia spectrum disorders present a number of challenges for clinicians. However, careful evaluation of the quality of symptom presentation, alongside the presence/absence of hallmark behaviors, can inform clinical decision-making and treatment decisions.

120.105 105 Shared Social Deficits in Autism Spectrum Disorders, First Episode Schizophrenia and Ultra High Risk for Psychosis Patients. E. Olsen*[1], M. Solomon[2], M. Minzenberg[1], J. D. Ragland[1], S. Ursu[1], J. H. Yoon[2], T. A. Niendam[1] and C. S. Carter[2], (1)*Imaging Research Center*, (2)*MIND Institute, Imaging Research Center*

Background:

Individuals with autism and schizophrenia spectrum disorders exhibit similar social, language, and repetitive behavior symptoms. However, there have been few studies comparing specific differences in these domains in individuals with autism spectrum disorder (ASD), versus those at ultra high risk for developing psychotic disorders (UHR) or for those with first episode schizophrenia (FE). This work has implications for understanding the comparative neurobiology of these disorders, for identification of precursors to psychosis and risk prediction, and for intervention.

Objectives:

The first goal of the study is to distinguish behavioral profiles of ASD, FE, and UHR across domains of reciprocal social interaction, structural and pragmatic language, and sensory/motor symptoms. The second goal is to begin to develop hypotheses about shared genetic and neurobiological mechanisms in ASD, schizophrenia spectrum, and other neurodevelopmental disorders. Finally we seek to consider dimensional rather than categorical approaches to characterizing symptomatology.

Methods: Four groups of 15 patients aged 12-18 diagnosed using gold standard measures as being ASD, UHR, FE, or typically developing (TYP) were ascertained from a clinically referred sample. Parents completed common autism research measures including the Social Communication Questionnaire, the Social Responsiveness Scale, the Children's Communication Checklist-2, and the Short Sensory Profile.

Results:

Based on SCQ, 6% and 7 % of each UHR and EPP cohorts respectively exhibited symptoms consistent with an ASD diagnosis. On the CCC-2, ASD demonstrate the highest level of global language impairment, however UHR and FE evidenced intermediate levels of impairment between ASD and TYP. UHR and FE exhibited more scripted language, less coherent speech, and increased language context violations relative to TYP. UHR resembled ASD in their tendency to talk repetitively about topics without regard for listener interest, while FE resembled ASD in relational aspects of communication as well structural language production. On the SRS, FE and UHR demonstrated similar impairments in reciprocal social behavior to ASD with a reduction in social motivation. ASD and FE were similarly impaired in lack of social awareness conversational skills, and autistic mannerisms. On the Short Sensory Profile, ASD, FE, and UHR shared comparable levels of sensitivity to Movement, Taste/smell, and increased Sensory Seeking behaviors while ASD and FE demonstrated similar low levels of energy.

Conclusions:

In this pilot sample, UHR and FE had about a 7% prevalence of ASD as determined by SCQ, however UHR and FE show symptoms that are generally of intermediate severity to TYP and ASD. Notable exceptions are that EPP and ASD share deficits in social awareness, conversational skills, autistic mannerisms, and low energy. UHR, unlike FE, show inappropriate social initiations comparable to ASD. While ASD tend to display worse language, social, and sensory/motor symptoms than other groups, specific impairments in social relational aspects of communication and some elements of sensory/motor atypicalities are similarly impaired in UHR and FE. Given the similarity of social and pragmatic language impairments across the ASD, UHR, and EP cohorts, social intervention and occupational therapy strategies for ASD may also be appropriate and useful for UHR and FE.

120.106 106 Are Social Deficits Content Dependent? Wason Selection Task Performance in ASD and Schizophrenia.

R. J. Sullivan[1], M. Solomon*[2], M. Minzenberg[3], J. D. Ragland[3], J. H. Yoon[2], S. Ursu[3], E. Ermer[4] and C. S. Carter[2], (1)*California State University, Sacramento*, (2)*MIND Institute, Imaging Research Center*, (3)*Imaging Research Center*, (4)*Mind Research Network*

Background:

The Wason Selection Task (WST) is a test of deductive reasoning based on the logical problem "if *p* then *q*". Performance on the WST is demonstrably sensitive to the context in which the problem is presented, particularly, that respondents perform significantly better on the task if it is presented as a rule violation of a social contract, than when it is presented as a purely descriptive problem without a social-contract condition. An influential interpretation of the conditional nature of WST performance is that it reflects content-dependent cognitive processes sensitive to violations of social rules (a neo-Darwinian perspective proposing domain-specific modularity in social cognition).

Objectives:

WST performance has been assessed in individuals with frontal lesions and schizophrenia, but not in individuals with autism spectrum disorder (ASD). Social deficits are prominent in both ASD and schizophrenia and the conditional sensitivity of WST performance makes it an ideal test of continuity, or lack thereof, of social cognitive performance in ASD, schizophrenia and typical development.

Methods:

Data gathering is proceeding in three groups: adult ASD participants with Autism Diagnostic Observation Schedule-Generic Module 4 scores above the ASD cut of, participants with schizophrenia diagnoses, and typically-developing controls. Participants are responding to five WST social-contract, five precautionary, and five descriptive problems (precautionary tasks are similar in difficulty to social-contract tasks but are hypothesized to utilize different cognitive resources; descriptive tasks lack social contract or precautionary conditions). Each WST is presented on a computer screen as a four-card task with two yes/no respondent choices for each card. IQ is assessed using the full-scale WASI.

Results:

Preliminary results indicate that WST social-contract performance is relatively impaired in participants with ASD when compared to

participants with schizophrenia and typical development, and that social-contract performance and General IQ are correlated in participants with ASD, but not in schizophrenia and typical development.

Conclusions:

We will interpret our results and discuss whether social cognition is content dependent and differently impaired in ASD relative to other mental disorders characterized by social deficits (that content-dependent cognitive processes sensitive to social-rule violations will be relatively impaired in ASD). We will discuss whether ASD participants are using other cognitive resources to solve the WST problems reflected in an apparent relationship between IQ and WST performance. In contrast to the patterns emerging in the ASD data, we will consider whether content-dependent cognitive processes sensitive to social-rule violations are intact in schizophrenia and typical development, and are independent of IQ.

120.107 107 Creating the Digital Melting Pot: Lessons from a Web-Based National Autism Registry and Research Project. A. R. Marvin*, K. Law and P. Law, *Kennedy Krieger Institute*

Background:

Autism spectrum disorder (ASD) studies are often limited to those living near research centers (usually located in larger metropolitan areas) and who are available during the work day. Web-based research studies offer an opportunity to expand access to research initiatives. According to the *Pew Internet & American Life Project Networked Families* (2008) report, 94% of married-with-children and 87% of single-parent families have home internet access. The *Public Libraries and the Internet 2008* report (ALA) notes that 98.9% of public library branches (including 100% "rural, high poverty") offer public Internet access. Also, internet access is frequently available in the workplace.

Objectives:

To compare participation of families of children with ASD (age <18) enrolled in a web-based national autism registry (Interactive Autism Network; IAN) across gender, ethnicity, race, prior research participation, and the urban-rural continuum.

Methods:

8606 parents of children with ASD provided demographic, medical, and educational data on themselves and their 8767 affected children (82.3% male). Completion rates of parent surveys were compared by gender, ethnicity (Hispanic-to-non-Hispanic), race, and urbanicity. Affected child participation by ethnicity and race was compared to NSCH 2003 data. Parental participation by urbanicity was analyzed using the 2006 NCHS Urban-Rural Classification Scheme (NCHSUR).

Results:

Mothers (88.4% of participating parents) were more likely to complete the parent questionnaire than fathers (86.4% to 83.0%, p=.004). 5.7% of parents and 7.7% of affected children (NSCH 2003 CI95%= 6.1%,11.2%) were Hispanic. Hispanic parents were less likely to complete the parent questionnaire than non-Hispanic (82.8% to 86.2%, p=.03) and affected Hispanic children were less likely to have a completed affected child questionnaire (58.8% to 66.0%, p<.001); this is likely due to language issues. 9.6% of parents and 13.6% of affected children (NSCH 2003 CI95%=13.6%,20.6%) were non-white and/or multiracial. Non-white/multiracial parents were less likely to complete the parent questionnaire than whites (80.0% to 86.7%, p<.001) and affected non-white/multiracial children were less likely to have a completed affected child questionnaire (56.4% to 66.9%, p<.001). The average participation rate (per million population count) across the six NCHSUR categories was 28.1. Smaller metro and micropolitan areas had participation rates comparable to that figure; however, the "large metro fridge" area had a much higher participation rate (47.5) and the "large central metro" and "non-core" (i.e., rural) areas had much lower participate rates (<20). There was no difference between the completion rates over NCHSUR categories except for "small metro", which had a higher completion rate (89.6% to 85.6%, p=.001). Of those affected children participating in IAN, only 13.7% had ever participated in a prior research study. There was no difference in prior research participation based on ethnicity, but fewer non-white/multiracial compared to white affected children had participated in a prior study (8.2% to 14.2%, p<.001) and fewer affected children living in small metro/micropolitan/rural area compared to large/medium metro areas (9.7% to 15.0%, p<.001).

Conclusions:

The internet has brought research opportunities to many families with ASD, most for the first time; however, societal issues (notably the absence and lower active participation of fathers) must also be addressed.

120.108 108 Vocalizations in Autism Spectrum Disorders Between 18 and 24 Months. A. M. Plumb*[1], A. M. Wetherby[2] and S. Randall[2], (1)*Auburn University*, (2)*Florida State University*

Background: Since there is currently no biological marker for ASD, there is a need for research into possible early behavioral markers. Few studies have investigated vocal patterns in children with Autism Spectrum Disorders (ASD) under 24 months of age.

Objectives: The purpose of this prospective, longitudinal study of the FIRST WORDS Project was to describe differences in vocalizations within and outside of communicative acts produced by 18-24 month old children with ASD, developmental delay (DD), and typical development (TD). In addition, for children with ASD, concurrent and predictive relationships between vocalizations and developmental level were investigated.

Methods: Videotapes of Communication and Symbolic Behavior Scales (CSBS) Behavior Samples for 125 children between 18 and 24 months of age (50 ASD, 50 TD, and 25 DD) were analyzed to obtain precise measures of vocalizations. Transcribable vocalizations (TVs) were coded to describe phonetic complexity and number of syllables. Nontranscribable vocalizations (NTVs) were coded according to specific categories of typical and atypical sounds. Social, speech, and symbolic composites were obtained from the CSBS (mean = 21.1 months) and Verbal Developmental Quotients (VDQ) were obtained from the Mullen Scales of Early Learning (MSEL; mean = 36.8 months).

Results: Children with ASD used a significantly lower proportion of vocalizations with consonants than children with TD. In addition, children with ASD used a significantly higher proportion of atypical NTVs than children with TD and a significantly higher proportion of distress NTVs than both children with TD and DD. For the ASD group, the frequency of vocalizations and the frequency of TVs correlated significantly with developmental levels both concurrently and at 3 years of age. In addition, communicative vocalizations late in the second year were found to uniquely predict expressive language outcome at age 3 over and above noncommunicative vocalizations.

Conclusions: By 18 to 24 months of age many vocalization measures significantly differentiated children with ASD from children with TD, with a higher proportion of distress vocalizations differentiating children with ASD from both children with TD and DD. The importance of communicative vocalizations for later language development is highlighted by the results of this investigation.

120.109 109 Relationship Between Atypical Sensory Behaviors and Socialization in Toddlers with Autism Spectrum Disorders. R. S. Oti*[1], D. Tracy[1], W. Guthrie[2] and C. Lord[2], (1)*University of Michigan Autism & Communication Disorders Center (UMACC)*, (2)*University of Michigan*

Background: Research has shown that while not unique to autism spectrum disorders (ASD), unusual responses to sensory stimuli are more common among individuals with ASD than among typically developing individuals or individuals with nonspectrum developmental delays. While studies vary in terms of which sensory modalities and behaviors are examined, one of the most consistent findings is the increased rate of hyporesponsiveness to sensory stimuli among individuals with ASD. In addition, one study found that hyporesponsiveness to social stimuli specifically differentiated the children with autism from PDD-NOS, suggesting that there may be a relationship between the increased social impairment in autism and atypical sensory responses. Few studies, however, have examined the relationship between unusual sensory responses and the core characteristics of autism. A relationship between unusual sensory symptoms and impairments in socialization could be hypothesized based on the results of previous studies that suggest a correlation between increased autism severity and increases in unusual sensory responses as well as research in the field of personality psychology, which has found connections between sensory response style and extroversion/introversion.

Objectives: The aim of the present study was to examine the relationship between atypical sensory responses and socialization among a group of toddlers with ASD, taking into consideration differences in NVIQ, age, and diagnosis.

Methods: Forty-nine participants were assessed multiple times between the ages of 12 months and 36 months. The average number of assessments was 3.8, with a range of 1-15. The Toddler Sensory Profile (TSP) was used to measure responses to sensory stimuli and the Autism Diagnostic Observation Schedule (ADOS), Autism Diagnostic Interview-Revised (ADI-R), and Vineland Adaptive Behavior Interview were used to assess socialization. Effect of unusual sensory responses on socialization was examined using general linear modeling and linear mixed modeling.

Results: Preliminary analyses indicated that there were significant correlations between ADOS Social Affect domain scores and TSP sensory scores. However, after controlling for age, NVIQ, and diagnosis, there was no relationship between the ADOS Social Affect algorithm scores and scores on the TSP. There was a significant effect of Low Registration, Sensory Sensitivity and Sensation Avoiding on ADI-R Reciprocal Social Interaction Domain scores and Vineland Socialization Domain Standard Scores, even after controlling for NVIQ, age, and diagnosis.

Conclusions: Results indicated that there is a relationship between sensory behaviors and socialization, however, the effect that atypical sensory behavior has on socialization is moderated by whether or not NVIQ and diagnosis are controlled for and how socialization is measured.

120.110 110 Superior Visual Search in 3 Year Old Children with Autism. M. O'Riordan[1], K. Peabody*[1], C. Allison[1], S. Baron-Cohen[1], P. Gerhardstein[2] and G. Iarocci[3], (1)*University of Cambridge*, (2)*Binghamton University*, (3)*Simon Fraser University*

Background: Perceptual disturbances in autism have long been documented and the visual search task has been used to provide empirical demonstrations of this anomaly. Studies have shown that superior visual search in autism is a developmentally stable feature of the disorder from children aged 7 years through to adulthood. Objectives: This study investigated visual search performance of young children with autism relative to typically developing matched controls to explore the stability of superior visual search in autism in early development. Methods: The performance of 3 year old children with autism on a modified visual search task was compared to that of a group of age matched and a group of developmentally matched typically developing control participants. A nonverbal shaping procedure was used to train participants to touch the screen location where they found a target item. On each trial a target item was presented among a varied number of distractor items. The stimuli were presented using a touch screen and the participants reaction times to touch the target item together with accuracy were recorded. Correct responses were rewarded with a short film clip. Results: The mean response time of the participants with autism to locate the target item at the largest display size was significantly faster than those of either of the control groups. Performance was comparable at small display sizes. Importantly accuracy rate of the autism group didn't differ from that of the control groups. Conclusions: Superior visual search in autism is developmentally stable from 3 years of age through to adulthood.

120.111 111 Optimal EIBI Outcomes for Autism Spectrum Disorders: An Analysis of Learning Rate and Treatment Hours. D. Granpeesheh, D. R. Dixon*, J. Tarbox, A. M. Kaplan and A. E. Wilke, *Center for Autism and Related Disorders*

Background: Early intensive behavioral intervention (EIBI) has been shown to effectively remediate some cases of autism. However, few studies have evaluated the importance of various factors, such as number of treatment hours per month, on treatment outcomes.

Objectives: To evaluate the relationship of treatment hours and participant age with the rate of learning within an EIBI program.

Methods: The present study evaluated treatment progress for 257 children receiving EIBI services. Multiple regression analyses were conducted to predict treatment progress based upon the number of monthly treatment hours received and the participant's age.

Results: Results indicated that each of these variables were significant predictors and accounted for considerable portions of the observed variance. Further, results indicate that younger participants showed a greater benefit from increased treatment hours when compared to older participants.

Conclusions: These data indicate that for children between 2 and 7 years of age, there was a significant increase in new skill acquisition with increased treatment hours. Further, there was not

a point of diminishing returns. These data highlight two factors that are important for treatment providers to manipulate on a system-level to achieve optimum treatment outcomes.

120.112 112 Preschool Social Skills Intervention for Children with Autism Spectrum Disorders: a Child Directed Approach. J. L. Mussey*[1], L. G. Klinger[1], E. M. Griffith[2], A. Williams[1], H. Noble[1], T. Perez[2], S. McCurry[1] and T. N. Holtzclaw[1], (1)*University of Alabama*, (2)*University of Alabama at Birmingham*

Background: Impaired social communication skills including delayed imitation, turn taking, and pretend play are some of the earliest symptoms of ASD. These impairments have been related to later difficulties in language development, play skills, and social relationships. Although adult-directed early intensive behavioral intervention approaches used in most preschool autism education settings have been shown to increase IQ and language abilities, they have not been shown to improve social skills (Kasari et al., 2006). Thus, there is a need for social skills intervention programs that utilize more child-directed intervention approaches.

Objectives: To design a child-directed social skills curriculum that can be implemented by a variety of social interaction partners within a preschool (teachers, speech therapists, or peers with typical development) or home setting (parents or siblings). This child-directed intervention therapy program was developed to target spontaneous imitation, turn-taking, joint attention, and social reciprocity in preschoolers with ASD. The goals of this program include increasing the child's attention to other people, increasing the child's eye contact and ability to combine eye contact with sounds or words, increasing the child's ability to learn through imitation, increasing the child's turn-taking during play, and increasing the child's playfulness when interacting with others.

Methods: Thus far, nine children (chronological ages 27-55 months) have completed a multiple baseline design intervention program. The program consisted of a pre-assessment, 4 to 8 free play baseline sessions, 10 twice weekly 30 minute intervention sessions, and a post-assessment. This intervention contained 3 phases that built on each other: imitation in which the adult imitated the child, turn-taking in which the adult imitated the child after pausing briefly to create a turn-taking game, and joint attention in which naturalistic rewards were provided when the child made a spontaneous nonverbal or verbal request for an object. Outcome was evaluated by measuring imitation, joint attention and turn-taking changes from pre- to post-treatment using the Early Social Communication Scales (ESCS), the Screening Tool for Autism in Two-Year-Olds (STAT), and the Motor Imitation Scale. Additionally, targeted probes were administered at the beginning and end of each therapy session.

Results: Preliminary results from the pre- to post-treatment data indicate significant increases in spontaneous (i.e., child directed) social skills. Specifically, ESCS measures of gaze shifts, vocalizations, and gestures to initiate joint attention and STAT measures of turn-taking increased significantly from pre- to post-treatment. Preliminary results indicate no significant changes on measures of adult directed social skills (i.e., responses to adult bids for joint attention or imitation). Analyses are ongoing for measures collected during each therapy session.

Conclusions: Preliminary results indicate that a developmentally-based child-directed intervention therapy program for children with ASD has a positive impact on the development and use of spontaneous early social skills. The fact that adult directed behaviors did not improve during the intervention suggests that this intervention has a specific effect on the type of child directed skills that were targeted. Future research is needed to examine the effectiveness of teaching parents and peers these intervention techniques.

120.113 113 Modified Milieu Therapy in the Natural Environment with Young Children with Autism. G. R. Mancil*, *Kelly Autism Program at Western Kentucky University*

Background: There is concern about the generalizability and maintenance of traditional FCT procedures. Objectives: Determine the effectiveness and efficiency of FCT with milieu procedures on decreasing aberrant behaviors, increasing communication mands, and increasing spontaneous communication with children with ASD. Methods: The subjects were referred by a local autism center that provides services for children with autism spectrum disorder and their parents. The subjects' diagnosis of ASD was confirmed by a review of records and the completion of the ADI-R. A functional analysis was completed to identify the function of each subject's aberrant behavior. The subjects were then taught picture communication using milieu

therapy procedures in play routines in their homes. The researcher trained the parents who then provided training to their children. Sessions were videotaped, coded, and then graphed using a multiple baseline format. Results: The subjects' FAs indicated a tangible function. The subjects obtained efficient use of three picture communication cards within 30 five-minute session blocks. Aberrant behavior decreased to zero and latency to respond to an opportunity leveled at 2 seconds. Further, two of the three subjects' verbal vocabulary increased on average from two words to 56 words. The complexity (i.e., number of words paired together) of their verbal speech also increased from one to four on average. In addition, these results maintained over time and generalized to the classroom for each subject. Conclusions: Findings of this study show the utility of milieu procedures in FCT to simultaneously decrease aberrant behaviors, increase communication mands, increase the diversity and complexity of verbalizations, and increase levels of maintenance and generalization.

120.114 114 Joint Effects of Nonverbal Accuracy and Nonverbal Processing Speed on Social Functioning among Children with Autism-Spectrum Disorders and Their Typically-Developing Peers. C. McKown*, N. M. Russo and M. Lipton, *Rush University Medical Center*

Background: Nonverbal accuracy, or the ability to infer others' emotions from nonverbal cues such as facial expressions, is an important contributor to social success. In naturalistic settings, nonverbal cues are displayed quickly and change rapidly. However, the speed with which children encode nonverbal information about others' emotions is an under-studied area. As yet, for example, it is unknown whether children with autism-spectrum disorders (ASDs) process nonverbal information at the same pace as their typically-developing (TD) peers. It is also unknown whether nonverbal processing speed explains a significant increment in the variance of children's social functioning, over and above nonverbal accuracy. **Objectives:** The objective of this study is to examine the relationship between nonverbal accuracy, nonverbal processing speed, and social functioning among ASD and TD children. We hypothesize that ASD children will score lower on measures of nonverbal accuracy and process nonverbal cues more slowly than their TD peers. We also hypothesize that nonverbal processing speed will predict a significant increment in teacher-reported social functioning, over and above nonverbal accuracy alone. **Methods:** A total of 160 TD children and 20 children with ASDs ages 5 to 14 completed multiple tests of affect recognition. Accuracy and processing speed (reaction time) were recorded. Regression procedures were used with the TD sample to estimate expected means for accuracy and reaction time at each age. In addition, expected variability around those regression estimates was computed. The distance in standard deviations from the expected mean for each child's age was then calculated. **Results:** Children with ASDs process nonverbal information more slowly than their TD peers. In addition, the relationship between nonverbal accuracy and teacher-reported social functioning depends on nonverbal processing speed. Specifically, children who process nonverbal information slowly *and* inaccurately are substantially less well-liked than children in possession of nonverbal processing speed, nonverbal accuracy, or both. Overall, nonverbal accuracy, nonverbal processing speed, and an accuracy by speed interaction term explain significantly more variance in social functioning than nonverbal accuracy alone. **Conclusions:** Nonverbal processing speed plays an important role in social functioning and is impaired among children with ASDs. Further attention to this dimension of nonverbal processing is needed.

120.115 115 Grammatical Aspect Is a Strength in the Language Comprehension of Young Children with Autism. L. Naigles*, G. Jaffery, J. Piotroski and D. Fein, *University of Connecticut*

Background:

Grammatical abilities of children with autism show strengths in clausal syntax; for example, children with autism understand word order before they produce it, and use sentence frames to learn about verbs (Tager-Flusberg, et al., Swensen et al.). Less is known about their comprehension of grammatical morphemes. Some research has found that children with autism have difficulties with grammatical tense and aspect (e.g., the "-ing"/"-ed" distinction); however, these findings have relied on production data, which can be unreliable in a disorder in which children are disinclined to speak (Roberts et al.).

Objectives:

We use intermodal preferential looking (IPL) to assess how/whether young children with autism *understand* tense/aspect markers.

Methods:

Children are tested every four months in this longitudinal study. Initially, children had a mean age of 33 months, had begun intensive therapy, and had language scores comparable to 20-month-old typical children. At Visit 5, when the children first viewed the tense/aspect videos, they averaged 49.6 months of age and produced on average 40% of the words on the CDI checklist. Their mean age-equivalents on the scales were 32 months (Communication) and 37 months (Motor). They also viewed the tense/aspect videos at Visit 6, when they averaged 53.9 months of age and produced on average 50% of the words on the CDI checklist. Their mean age equivalents on the Mullen at Visit 6 were 37.3 months (Visual Reception), 35.8 months (Fine Motor), 36.3 months (Receptive Language) and 34.15 months (Expressive Language).

The tense/aspect video contrasted two familiar events, one presented as ongoing (a girl washing a dolly) and the other presented as completed (the girl finished washing the dolly). During the control trial, both events were presented simultaneously with a non-directing audio ("She is on both screens!"). During the test trials, the audio presented the verb with the '-ed' suffix (first block; e.g., "She washed the dolly") and '-ing' suffix (2nd block; "She's washing the dolly"). At Visit 5, two verbs (*wash, drink*) were presented in each block whereas at Visit 6, four verbs (*wash, drink, pick, draw*) were presented in each block. Children's eye movements were coded off-line. Children should look longer to the matching screen during the test trials compared with the control trials.

Results:

The children looked significantly longer at the matching scenes during the test trials (60.8%) than during the control trials (50.5%) for both suffixes at both visits (Visit 5: $t(10) = 2.06$, $p = .03$; Visit 6: $t(10) = 2.08$, $p = .03$). Thus, they demonstrated understanding that verbs with the "–ing" suffix describe ongoing actions and verbs with "past/–ed" describe completed actions. Typically developing children show the same understanding around 30 months of age (Wagner, et al.). No correlations were found between tense/aspect understanding and standardized test performance.

Conclusions:

Young children with autism are able to contrast the aspectual nature of events based on the grammatical marker of the verb; therefore, their difficulties with producing these markers are not entirely due to a lack of knowledge.

120.116 116 The Role of the Self in Autobiographical Memory in Adults with Autism. L. Crane*, L. Goddard and L. Pring, *Goldsmiths College, University of London*

Background: In typical adults, self-referential information receives privileged encoding, which facilitates subsequent memory retrieval. This is especially true of information relating to personal goals (Conway & Pleydell-Pearce, 2000). However, several studies have shown that the 'self-reference effect' in memory is either attenuated (Lombardo, Barnes, Wheelwright & Baron-Cohen, 2007) or completely absent (Toichi, Kamio, Okada et al., 2002) in adults with autism. Accordingly, autobiographical memory (memory for personally experienced events and self-related information) has also been found to be impaired in this group (e.g. Crane & Goddard, 2008).
Objectives: The main aim of the current study was to assess whether the autobiographical memory difficulties in adults with autism were related to difficulties in using the self as an effective memory cue. A further aim of the study was to assess both specific autobiographical memories (memories of individual events, e.g. 'my wedding day') and general autobiographical memories (memories of repeated occurrences, e.g. 'going on holidays'), to identify whether one or both of these aspects of memory was impaired in autism.
Methods: 28 adults with autism and 28 comparison participants (matched for age, gender and IQ) selected a series of life-goals that they were currently pursuing from a list of 50 commonly pursued goals (taken from Moberly & MacLeod, 2006). These goal items, and a selection of non-goal items, were then used as memory 'cues' on a task assessing specific autobiographical memory retrieval, and on two tasks focused on the retrieval of general autobiographical memories.
Results: Overall, the adults with autism took significantly longer to access both specific and general autobiographical memories than the comparison group; this delay was particularly pronounced for specific memory retrieval. Regarding the hypotheses concerning the self and memory, it was found that, as predicted, goal cues facilitated both specific and general

autobiographical memory retrieval in the comparison group. In the autism group, goal cues were only found to enhance the retrieval of general autobiographical memories; no relationship was found between goal self-relevance and specific autobiographical memory retrieval in the adults with autism.
Conclusions: In line with the results of previous studies (e.g. Crane & Goddard, 2008), the current results suggest an autobiographical memory deficit in adults with autism. This deficit was found to be particularly pronounced for specific autobiographical memory retrieval; in contrast, retrieval of general autobiographical memories was only slightly delayed in the autism group. Interestingly, the adults with autism were able to use the self to facilitate general, but not specific, autobiographical memories. This suggests that the failure to use the self as an organisational system may be one factor underlying the specific autobiographical memory difficulties in autism. Specific autobiographical memories (opposed to general autobiographical memories) serve several important social functions; aiding in social problem-solving (Goddard, Dritschel & Burton, 1996), in providing information for social communication (Cohen, 1989) and in the formation and maintenance of social bonds (Pillemer, 1992). The specific autobiographical memory impairments in autism may therefore contribute to some of the social deficits observed in this group.

120.117 117 Weak Central Coherence and Resistance to Distractor Inhibition in Children with Autism. N. C. Adams* and C. Jarrold, *University of Bristol*

Background:

Inhibition tasks that require resistance to distracting stimuli, such as Flanker Tasks, often reveal a deficit in children with autism (Christ et al., 2007). However, on the classic Stroop task, a task requiring suppressing a prepotent response, children with autism appear to have intact inhibition, performing faster than typically developing children (Bryson, 1983). These data may reflect a distinction between prepotent response and resistance to distractor inhibition (Friedman & Miyake, 2004), which may be differentially impaired in autism.

Objectives: : The current study investigated the possibility that children with autism may be impaired in resistance to distractor, while remaining unimpaired in prepotent response, inhibition.

Methods:

Three groups were assessed, 17 children with autism, 17 children with learning disabilities, and 17 typically developing children. Groups were matched using the Raven's Coloured Progressive Matrices Test. All children were given 4 tasks, 2 of which were prepotent reponse tasks (antisaccade task, stop-signal task) and two of which were resistance to distractor tasks (flanker task, and abstract shape task). During the antisaccade task, children identified the direction of arrows that appeared on uncued sides of the screen. During the stop-signal task, children categorized pictures as animals or non-animals except when they heard a beep, where they were instructed to withhold response. For the Flanker task, children identified the direction of a central arrow, which appeared flanked with congruently or incongruently pointing arrows. Finally, in the abstract shape task children saw two green shapes side by side, sometimes with the left green shape overlapping a different red shape. Children were asked to determine whether the two green shapes matched.

Results:

For the antisaccade task, the groups did not differ significantly in either time to make a response, $F(1, 48) < 1$, or number of errors, $F(1, 48) < 1$. Similarly, on the stop-signal task there was no group effect on number of prepotent errors made, $F(1,48) = 1.63$, $p = .21$. Interestingly, results from the 2 resistance to distractor tasks showed that while the groups performed comparably quickly on the tasks, $F(1,48) < 1$, children with autism made significantly less errors on the flanker task in the incongruent condition, $F(1,48) = 4.29$, $p < .001$. The same trend, although not significant, was evident in the distractor condition of the shape task, $F(1,48) = 1.71$, $p = .19$.

Conclusions:

These findings suggest that individuals with autism show intact inhibition, and certainly there is no evidence for problems on the prepotent response inhibition tasks. However, while individuals with autism were as rapid as controls on the two resistance to distractor tasks, they

made fewer errors in the conditions in which distractors were incongruent. This finding can clearly be explained in terms of a weak bias to central coherence in autism, which in this case makes competitor items in the global display less distracting. This raises the question of whether individuals with autism would show inhibitory deficits on such tasks if they were made equally distracting for them as controls.

120.118 118 Increasing Social Responsiveness in Children with Autism: a Comparison of Music and Non-Music Interventions. E. Finnigan and E. Starr*, *University of Windsor*

Background: Many children with autism have difficulty engaging in social interaction with others. One intervention that has been used to increase social skills in children with autism is music therapy, an established healthcare profession that uses music to address physical, emotional, cognitive, and social needs of individuals of all ages (American Music Therapy Association, 1999).

Objectives: Because music therapy is being used on an increasing basis for children with autism, this study sought to determine the effect of this intervention on the social responsive behaviours of a child with autism. Specifically, it was hypothesized that the child would engage in a greater number of social responsive behaviours and fewer social avoidance behaviours in the music therapy condition than in the non-music condition in which the same activities were done, but without music.

Methods: This research used a single subject design with alternating treatments to evaluate the effects of both music and non-music interventions on the social responsive behaviours of a preschool child with autism. The non-music and music interventions were designed and implemented in an identical fashion the only difference being the addition of music. Each intervention used toys (e.g., non-music = maracas, stacking cups and plastic animals; music = car, drum, and ball) as a means to offer the child opportunities to engage in social responsive behaviours using either a spoken script or a sung melody. Social responsive behaviours were defined as eye contact, imitation, and turn-taking whereas social avoidant behaviours where defined as pushing the toy away, pushing the adult away and moving away, all which were measured in terms of frequency. An equal number of both interventions were randomly conducted with the child in an alternating manner and after a total of 12 treatment sessions.

Results: Results indicated that the music therapy intervention produced a higher frequency of each of the three social responsive behaviours. Furthermore, no instances of social avoidant behaviours occurred in the music condition. As a result, the music intervention was then applied to the non-music toys and over the course of 7 additional sessions, higher frequencies of the three social responsive behaviours were observed.

Conclusions: It is suggested that because music was a preferred activity, the participant was motivated to engage in more social responsive behaviours during the music intervention. The fact that music therapy appears to be motivating for a young child with autism suggests the importance of incorporating music therapy interventions into programming for pre-school children with autism

120.119 119 Selective Attention and Perceptual Load in Autism Spectrum Disorders. A. Remington* and J. Swettenham, *University College London*

Background: When we focus our attention on an aspect of the environment it is important to be able to ignore potentially interfering distractors (selective attention). Ignoring distractors though is not always something that can be done at will, and it does seem that under some circumstances we process distractor information whether we like it or not (e.g. we hear our own name mentioned in a conversation we are not focusing on at a cocktail party). Recent research by Lavie (1995) has shown that the degree to which distractors are processed depends on how much of our finite attentional resource is allocated to the task we are focussing on (perceptual load theory).

Our previous research has examined the effect of perceptual load on selective attention within Autistic Spectrum Disorders (ASD). Previous studies suggest that individuals with ASD might find it difficult to ignore distractors (Burack et al 1994), although no studies have yet taken into account the perceptual load of the focus task. Our results showed that individuals with ASD continue to be affected by distractors at higher levels of perceptual load than typically developing controls. This suggests that there may be increased perceptual capacity in individuals with ASD

Objectives: Our previous studies use indirect measures (effect on reaction times) to draw conclusions regarding the extent of irrelevant distractor processing at differing levels of perceptual load. Such measures, however, cannot be used to infer whether the task-irrelevant

stimuli are consciously perceived. This study aimed to investigate this by using a dual-task paradigm (Macdonald & Lavie, 2008) to examine how the increased distractibility within ASD relates to conscious perception and awareness. Methods: Young adults with ASD and typically developing adults, matched for chronological age and non-verbal IQ, performed a dual-task paradigm where it was necessary to detect the presence of an expected critical stimulus that was presented offset from a central visual search task. The perceptual load of the central task was varied. Results: Preliminary results suggest that individuals with ASD are able to consciously perceive the critical stimulus at higher levels of load than typically developing control individuals. Conclusions: These findings reinforce the view that individuals with ASD have a greater perceptual capacity and imply that they can consciously perceive a larger number of visual stimuli at any given time.

120.120 120 Perception of Emotion in Musical Performance in Adolescents with ASD. A. K. Bhatara[1], E. M. Quintin*[2], E. Fombonne[3] and D. J. Levitin[3], (1)*University of California, Los Angeles*, (2)*Université du Québec à Montréal & Centre for Interdisciplinary Research in Music, Media, and Technology*, (3)*McGill University*

Background: Individuals with autism spectrum disorders (ASD) are impaired in understanding the emotional undertones of speech, many of which are communicated through prosody. Musical performance has similar prosodic aspects.

Objectives: The goal of this study was to examine the effects of within-performance timing and amplitude variation on the ability of adolescents with high-functioning ASD to understand emotion.

Methods: We created piano performances of Chopin nocturnes with varying degrees of emotional expressivity (by manipulating timing and amplitude variation) and asked 32 adolescents with ASD and 32 matched controls as well as 11 individuals with Williams syndrome to rate how emotional these manipulated excerpts sounded.

Results: The participants with ASD did not differentiate among the levels of emotional expressivity, demonstrating an impairment relative to the participants with Williams syndrome and the control group.

Conclusions: Participants with ASD are impaired at judging emotionality from musical performance.

120.121 121 Assessing Theories of Central Coherence and Perceptual Functioning with Music in ASD. E. M. Quintin*[1], A. Bhatara[2], H. Poissant[3], E. Fombonne[2] and D. J. Levitin[2], (1)*Autism Research Training Program, Université du Québec à Montréal*, (2)*McGill University*, (3)*Université du Québec à Montréal*

Background: Individuals with autism spectrum disorder (ASD) exhibit spared or enhanced perception and discrimination of local musical elements such as pitch (Bonnel et al., 2003; Heaton, et al., 1998). Although Foxton and colleagues (2003) reported that individuals with ASD can perceive musical contour, few studies have assessed global processing of music in ASD.

Objectives: To test central coherence (Happé & Frith, 2006) and enhanced perceptual functioning (Mottron et al., 2006) theories in ASD using musical stimuli. Although both theories recognize intact or enhanced local processing in ASD, the former theory stipulates that this will impede global processing whereas the latter suggest that global processing will be spared or enhanced.

Methods: Teenagers with ASD (N=22; age: Mean±SD= 13.2±2.1 years, FSIQ: Mean±SD= 97±17) and typically developing (TD) teenagers (N=22, age: Mean±SD= 12.1±2.3 years, FSIQ: Mean±SD= 108±12) with comparable verbal and performance IQ and musical knowledge and ability participated in the study. Participants were asked to solve a musical puzzle made of 5 plastic cubes, each playing a segment of a melody. In the first condition (creation), participants were asked to arrange the 5 blocks in the order they though sounded best. In the second condition (replication), participants listened to a musical excerpt twice and were asked to place the blocks in the order which would replicate the excerpt. The musical excerpts to be reconstructed were the same for both conditions and 5 excerpts, lasting 10-30 seconds, were presented in each condition.

Results: For both conditions (creation and replication), performance of participants with ASD was compared to performance of typically developing participants. There was no significant difference between groups (all $p<.05$) for time needed to solve the musical puzzles, number of pieces of the puzzle that were placed in the correct location, and number of pieces of the

puzzle that were placed in the correct sequence independently of location.

Conclusions: Although more evidence is needed to assess musical processing in children and teenagers with ASD, global processing in ASD does not seem to differ from typically developing children and teenagers. These results support the description of global processing suggested by the enhanced perceptual functioning theory.

120.122 122 Role of Pitch-Discrimination Abilities in Sequential Auditory Stream Segregation by Individuals with Asperger's Syndrome. C. Füllgrabe*, *University of Cambridge*

Background: Sensory reactions and perceptual abilities in individuals with autism spectrum disorder (ASD) seem to differ from those in typically developing individuals. Results from studies assessing perceptual functions in ASD led to the Enhanced Perceptual Functioning model (e.g. Mottron *et al*., 2006), postulating that ASD is characterized by better-than-normal perception of basic stimulus attributes, but worse-than-normal higher-level processing. Consistent with this model, enhanced discrimination of pitch, *i.e.*, the subjective percept of a pure-tone frequency, was observed in ASD, while speech identification, especially in noisy environments, can be degraded. However, so far, the link between pitch perception and auditory scene analysis has not been assessed behaviourally.

Objectives: To further test the hypothesis of enhanced pitch-discrimination abilities in ASD using a standard psychophysical procedure combined with different tasks, and to investigate the role of this basic auditory function in sequential auditory stream segregation.

Methods: Children with Asperger's syndrome (AS; age range = 12-16 years), age- and IQ-matched typically developing controls (TDC), and adult controls (AC) were recruited for five experimental sessions. Only participants with audiometrically normal hearing sensitivity were included. Frequency-discrimination thresholds for reference frequencies ranging from 250 to 4000 Hz were obtained in two different adaptive tasks, using a 2-interval, 2-alternative forced-choice procedure with feedback. First, participants had to indicate which of two successively presented pure tones (A *vs.* B) had the higher frequency (*i.e.*, pitch). Since this task assesses temporal-order judgement in addition to frequency discrimination, participants were also tested on a task requiring to indicate in which of two intervals, each composed of four successively presented pure tones, a change in frequency occurred (A-A-A-A *vs.* A-B-A-B). Subjective and objective measures of sequential auditory stream segregation were also obtained in the same participants, using pure-tone sequences (A-B-A-B… and A-B-A—A-B-A…, respectively). A-tones had a frequency of either 250 or 1000 Hz, whilst the B-tones had either the same frequency (no streaming; base line) or differed in frequency from the A-tones (measured in terms of the perceptually relevant scale of equivalent-rectangular bandwidths). Prior to data collection, participants received practice on all tasks and conditions during the initial three sessions to stabilize performance.

Results: Preliminary data obtained so far for six AS and three AC indicate that: (i) All participants improved markedly over the initial threshold runs on the first frequency-discrimination task, arguing against its diagnostic use (*i.e.*, without preliminary practice) for the assessment of pitch-processing abilities; (ii) Despite the age difference (and hence a potential maturational difference), AS showed, on average, adult-like frequency-discrimination thresholds; the comparison to data obtained in TDC will reveal if this sensitivity is better-than-normal for that age range; (iii) Under certain frequency separations between A- and B-tones, stronger sequential stream segregation was observed in AS than in AC, indicating that the pitch of pure tones may be a more salient streaming cues in this population.

Conclusions: The final results will be discussed in the light of the predictions of current models of affected perceptual functioning in autism.

120.123 123 The Social World of Autism: Perspectives from Adults on the Autism Spectrum. J. Singh*, *University of California, San Francisco*

Background: Despite the broad range of practices contributing to the understanding and meaning of autism, very little research has focused on the world as it is conceived, experienced and imagined by those on the autism spectrum. Rarely are narratives found in the literature that help scientist understand the heterogeneity within autism spectrum disorder (ASD) and the life experiences that contribute to how people with ASD come to understand this disorder. Furthermore, the construction and understanding of this disorder has been focused mainly on

children and not necessarily adults. The extent to which adults with ASD experience the social world may be very different than those practices involved in understanding ASD as either a childhood disorder, a psychological disorder, a genetic disorder, a neurological disorder, or a combination there of.

Objectives: The purpose of this research is to better understand the social world of adults identified or diagnosed on the autism spectrum. It will reveal how individuals identified or diagnosed with high functioning autism or Asperger's disorder describe different levels of silencing and suffering base on their life experiences, and the survival mechanisms they have used to help them transition into adulthood.

Methods: The data collection consists of 18 in-depth interviews with adults (ages 18-55 years old) who are diagnosed or identify with high functioning autism or Asperger's disorder. The participants were asked what they know about autism spectrum disorders, their experiences with or without a diagnosis, and the major challenges they have experienced in life.

Results: The silencing mechanisms apparent in this sample centered around communication and social interaction issues. Consequently, this was a cause for much of the suffering experienced by these adults in the form of anxiety, isolation and misinterpretation. Other suffering occurred through different forms of depression, compulsive behavior, and sensory stimulation. Survival mechanisms were based on different ways of learning how to cognitively perform in social situations, the ability to identify strengths and weaknesses, and the diagnosis and disclosure of being on the autism spectrum.

Conclusions: This study offers insight to the silencing, suffering and survival processes of adults on the autism spectrum. The social world experienced by participants in this study are much more proximal to the day-to-day life experiences in social interaction rather than complex practices that describe autism based on different forms of scientific and technical knowledge. Their advise to scientists studying autism is to focus more on how they can be contributing members to society by addressing who they are "now" and focusing on the many differences that exists among people on the autism spectrum.

120.124 124 Relationships Between Executive Functions and Temperament in High-Functioning Youth with an Autism Spectrum Disorder. L. Goodman*, J. Baker and S. A. Johnson, *Dalhousie University*

Background: Executive dysfunction is often cited as a central cognitive deficit in autism spectrum disorders (ASD; Pennington & Ozonoff, 1996). However, some studies of executive function (EF) in ASD have shown intact performance (Bryson, 1983) while others suggest impairments (e.g., Ozonoff, et al., 1991; Pascualvaca et al., 1998). In typically developing (TD) individuals, there is support for relationships between EF and temperament. For example, Gonzalez et al. (2001) found that activity level, impulsivity, and inhibitory control were related to Stroop Task performance. Interestingly, there is also mounting evidence for differences in temperament in ASD. Garon et al. (2008) found that high-risk infants (older sibling with ASD) later diagnosed with an ASD were distinguished from non-ASD infants by lower positive affect, higher negative affect and difficulty controlling attention. Similarly, Konstantareas & Stewart (2006) demonstrated that 'effortful control' best differentiated children with ASD from their TD peers. Objectives: In this study, our goal was to determine if performance on EF tasks is associated with temperament factors in youth with an ASD. Methods: Eleven high-functioning youths with an ASD and 11 TD participants matched for age (range = 8 – 18) and IQ, completed the Wisconsin Card Sorting Test (WCST) and the Stroop Task. One of three temperament questionnaires was administered: Temperament in Middle Childhood Questionnaire (ages 7 – 10, parent-report; Simonds & Rothbart, 2004); Early Adolescent Temperament Questionnaire (ages 9 – 15, parent-report; Ellis & Rothbart, 2001); or Adult Temperament Questionnaire (ages 16 and up, self-report; Rothbart, Ahadi, & Evans, 2000). We examined relationships between performance on EF tasks and attentional control, inhibitory control, and activation control (i.e., subscales comprising effortful control). Results: The ASD and TD group did not differ on their EF performance (WCST total standardized errors: ASD M = 51.3, control M = 47.2, $p > .1$; Stroop Interference total: ASD M = 31.7, control M = 34.3, $p > .1$). Moreover, the ASD group had lower scores than the TD group on the attentional control ($t = -2.32$, $p < .05$) and inhibition subscales ($t = -2.55$, $p < .05$), indicating less ability to control attention and inhibition. The groups did not differ on the

activation control subscale. For the TD group, more overall errors and perseverative responses on the WCST were associated with lower activation control (r = -.77 and -.88, respectively) and lower attentional control (r = -.69 and -.80, respectively). However, Stroop Interference scores were not related to any temperament subscale. For ASD participants, there were no associations between WCST performance and temperament data. However, better performance on the Stroop interference trial was significantly correlated with higher scores on the inhibition subscale (r = .71), indicating that a higher level of behavioural inhibition was associated with stronger cognitive inhibition. Conclusions: These preliminary data suggest that individuals with an ASD may differ from their TD peers with respect to how temperament is related to EF. Understanding relationships between EF and temperament may provide important insights into the variability of EF performance across individuals with an ASD.

120.125 25 Phenotypic Congruence in Multiplex Autism Families. J. Pandey*[1], K. Carr[2], A. D. Verbalis[2], M. Barton[2] and D. Fein[2], (1)*Children's Hospital of Philadelphia*, (2)*University of Connecticut*

Background: Clinical research investigating children with autism spectrum disorders (ASD) has yielded significant heterogeneity with regard to symptom severity and level of functioning. This complex clinical picture has contributed to difficulty in locating etiologically relevant genes. In order to better categorize this phenotypic variance and facilitate genetic research, much research has been devoted to studying multiplex cases of autism – families in which two or more individuals have been diagnosed with ASD. Research focused on assessing sibling concordance (non-twin pairs) based on level of functioning have yielded mixed results. Some studies have found little to no evidence for familial aggregation of IQ, verbal ability, or specific behaviors (Spiker et al., 1994), while others have found familial aggregation of measures of social communication, IQ, and adaptive behaviors (Szatmari et al., 1996; MacLean et al., 1999; Goin-Kochel et al., 2008). Objectives: The current study investigated the familiality of symptom severity, IQ, and adaptive functioning within non-twin, multiplex families, in which the younger sibling was identified through a screening instrument.Methods: Thirty-eight pairs of multiplex siblings affected by an autism spectrum disorder (ASD) were evaluated as part of a larger study on the early detection of autism in toddlers. The younger siblings of children already diagnosed with an ASD were ascertained on the basis of screening positive on the Modified Checklist for Autism in Toddlers (M-CHAT). Their older siblings were evaluated to confirm their previous diagnoses. Evaluations for all pairs included a battery of diagnostic, cognitive, and adaptive tests. Diagnoses were assigned based on the DSM-IV symptom checklist, completed using information from testing and clinical judgment. All children in this sample received a diagnosis of Autistic Disorder, Pervasive Developmental Disorder – Not Otherwise Specified (PDD-NOS), or Asperger's Disorder. For the purposes of this study, sibling pairs were compared across the domains of the ADOS, DSM-IV, Mullen, and Vineland Adaptive Behavior Scales.Results: Consistent with findings from an investigation of repetitive behaviors in multiplex siblings from our group (Carr et al., presented), intraclass correlations (ICCs) conducted between older and younger siblings in a pair indicate that multiplex siblings were more similar to each other across all domains on the measures of symptom severity, IQ, and adaptive functioning than were unrelated children. Conclusions: Our findings support those of Goin-Kochel et al. (2008) who found that siblings with ASD were more similar on measures of IQ and adaptive functioning than affected non-siblings. These results further suggest the importance of stratifying families by symptom severity and level of functioning when conducting genetic studies of autism. The fact that the same parent often served as respondent might have inflated the similarity within sib pairs, but would not be expected to affect the direct testing and observation measures. Possible effects of birth order and diagnostic classification (Autistic Disorder versus ASD) will also be discussed.

120.125 125 Advanced ToM Tests Which Consist of Visual and Auditory Modalities. M. Kuroda*[1], A. Wakabayashi[2], T. Uchiyama[3], Y. Yoshida[4], Y. Muramatsu[4], Y. Uno[4], Y. Hachiya[4], N. Hihara[5] and H. Fujioka[6], (1)*National Center of Neurology and Psychiatry*, (2)*Chiba University*, (3)*Otsuma Women's University*, (4)*Yokohama Psycho-Developmental Clinic*, (5)*Yokohama Tohbu Community Habilitation Center for Children*, (6)*Tsubasa Psycho-Developmental Clinic*

Background: High functioning (HF) adolescents and adults with autism spectrum disorder (ASD) can recognize others' simple mental states and pass the basic theory of mind (ToM) task, such as the first and second-order false belief tasks. Basic ToM tasks are not sensitive enough to detect ToM deficits in individuals with HF-ASD. Therefore,

various advanced ToM tasks have been constructed to measure those deficits. Also, recently there has been a concern about which is the predominant perception for the individuals with ASD to understand the mental states of others (Golan et al., 2006) .

Objectives: We constructed new advanced Visual and Auditory ToM tasks which could provide evidence of subtle social cognitive deficits in the individuals with HF-ASD. Moreover, our tasks were complex because they included many non-literal scenes with incongruent dialogue and mental states. This study was an attempt to understand the real mental state from only the visual modality (facial expression) or only the auditory modality (non-verbal aspects of speech: pitch/intonation/tone) independent of each other. Our other objective was to identify which modality, visual or auditory, was useful for individuals with ASD to understand the mental states of others.

Methods: The participants consisted of 21 adolescent and adult males with ASD (mean age = 24.5 years, mean VIQ = 104.5, PIQ = 98.4, FIQ = 101.8, mean Autism-Spectrum Quotient (AQ) = 33.4) and a control group of 50 male students recruited from Chiba University (mean age = 21.2). The advanced ToM Tests that were constructed for this research consisted of 41 video clips (3 seconds ~ 11 seconds in length) from the TV drama "Shiroi Kyotou", a story about malpractice in a famous Japanese medical school. One Visual task and one Auditory task were made for each corresponding clip. For the Visual tasks, the sound of the 41 scenes was deleted. For the Auditory tasks, the pictures of the 41 scenes were deleted. A word or a phrase which expressed the various and complex mental state was shown along with each video and sound clip. The participants were asked to judge if each word or phrase was appropriate or not for each scene.

Results: Comparing the correct answer rate, there were significant differences between the ASD group and the control group in the Auditory tasks ($p < .01$), but not in the Visual tasks. Also our results showed that the AQ score was negatively correlated with the performance in the Auditory task($r = -0.46$, $p < .05$).

Conclusions: Our Auditory tasks are useful to identify individuals with ASD. Also, mind-reading ability could be predicted from AQ. The results suggest that the visual modality is useful for the individuals with HF-ASD to understand the mental states of others in complex situations.

120.126 126 Social Engagement and the Pragmatics of Conversation in Autism. R. P. Hobson*[1], J. A. Hobson[1], J. Du Bois[2] and R. García-Pérez[3], (1)*Institute of Child Health, UCL*, (2)*University of California, Santa Barbara*, (3)*Musicaycolor Child Psychology Music Therapy Center*

Background:

Socio-cognitive approaches to language acquisition emphasize the importance of social experience for a child's ability to learn how to use words. Given that social relations involve affective as well as cognitive processes, how far might some of the pragmatic language deficits of children with autism be grounded in affective or other intersubjective aspects of communication?

Objectives:

The aim was to examine whether among children with autism, there are relations among impaired *social-affective* and/or *intersubjective* processes and atypicalities in the pragmatics of language use in conversation. We tested the specificity of such relations by assessing whether there were relatively spared structural aspects of language.

Methods: Participants were 12 children with autism between the ages of nine and 19 years with a mean verbal mental age of 6 years; 6 months (VMA range = 4 – 10 years) and 12 children without autism between the ages of 11 and 17 years with (VMA *M* = 6 years; 7 months, range = 4 – 9.5 years). Participants had each been videotaped in conversation with an adult for a previous study that yielded reliable ratings (on a five-point scale) of how 'emotionally connected' each participant was with the interviewer. For the present studies, we transcribed a standard three minutes of the interview for ratings by judges who were 'blind' to diagnostic groups.

Firstly, we rated how far participants' conversation manifested 'linkage with speaker's meanings' (i.e. with what the speaker intended, ICC = .64) and 'linkage with utterance meanings' (i.e. with the literal meanings of the words spoken, but not necessarily the intended message, ICC = .68).

Secondly, we employed a newly-devised form of Du Bois' approach to rating transcripts of

conversation for 'dialogic resonance', a measure focused upon intersubjectively configured aspects of dialogue. Independent raters achieved satisfactory reliability (ICC range = .57 to .89) in rating atypicalities in three aspects of speaker-hearer resonance – that is, three features of speaker-hearer intersubjective alignment manifest in language – namely, frame resonance with missing/incoherent expansion (e.g. Interviewer: 'What do you like most about yourself?' Participant: 'Most about myself is the teach'), taxonomic resonance (e.g. I: 'What sort of person are you?' P: 'A girl') and non-indexed alignment (e.g. I: 'Is it important to control it?' P: 'It is' [rather than: 'Yes, it is'].

Results: As predicted, (a) the groups differed in linkage with speaker's meanings, but not linkage with utterance meanings, and (b) for the children with autism, linkage with speaker's meanings correlated with emotional connectedness (r = .54) but not verbal MA (r = -.09), whereas for children without autism, it correlated with verbal MA (r = .41) but not emotional connectedness (r = -.43).

In addition, the groups were significantly different on a composite measure of these three atypicalities of intersubjective, dialogic linkage – even though in other respects, participants with autism demonstrated abilities to register and elaborate upon what the conversational partner had said.

Conclusions:

Children with autism show atypicalities in pragmatic linguistic adjustment during conversation that are intimately related to the children's limited affective/intersubjective engagement.

120.127 127 The Role of Learning in Visual Endogenous Orienting. O. Landry*[1], R. Nicolson[2] and J. B. Morton[1], (1)*University of Western Ontario*, (2)*The University of Western Ontario*

Background:

Children with autism have difficulties strategically directing their visual attention, exhibiting unusual looking behaviour when interacting with both people and objects. On laboratory experiments in which symbols, such as an arrow, are used as cues to direct attention, persons with autism require more time to make a response, though this is not affected by how much time is available to see the cue, or how fast children can press buttons to make responses.

Objectives:

The purpose of this project is to examine the ability of children with autism to use symbolic cues to guide visual attention. Two experiments were designed to examine the role of learning the cue-target relationship in visual orienting performance. In the first experiment, children with and without autism complete visual orienting tasks with cues that range from non-symbolic to arbitrary, where the cue-target association must be learned within the confines of the task. In the second experiment, children with and without autism complete a visual sequential learning task with increasing cues to aid performance.

Methods:

Data collection will begin in January; participants will include 20 children with and without autism ages 8-12. Experiment 1 examines learning in visual orienting tasks under conditions that vary in both type of representation and predictability of the cue. Children perform three computerised orienting tasks, with non-symbolic (peripheral flash), directional symbolic (central arrow) and arbitrary symbolic (central colour) cues. Targets appear on the left or right side of a computer screen in blocks of non-predictive (25% correctly cued) and predictive (75% correctly cued) conditions. Experiment 2 examines learning simple sequences in visual orienting under three different cuing conditions: no cue, implicit cue, and explicit cue. In the first task, targets appear one at a time in a quadrant of the computer screen in blocks of random sequence, clockwise sequence, and counter-clockwise sequence (No-Cuing). In the second task, the targets for each type of sequence appear on a different coloured background (Implicit Cuing). In the third task, children are told in advance which sequence occurs with each of the different coloured-backgrounds (Explicit Cuing).

Results:

The hypotheses of Experiment 1 are that children with autism will exhibit weaker orienting effects on the directional and arbitrary cue conditions, but intact performance on the non-symbolic cue condition, and that children with autism will be

less affected by the manipulation of predictability than matched typically developing children. The hypotheses of Experiment 2 are that children with autism will display a different learning curve than matched typically developing children, and that this difference will be most pronounced on the Implicit Cuing condition.

Conclusions:

If these hypotheses are supported, this will suggest that difficulties exhibited by children with autism on visual orienting are a function of difficulty learning the relationship between the cue and target.

120.128 128 Relationships Between Memory Performance and Intellectual Ability in Autism Spectrum Disorders. H. L. Phelan, J. H. Filliter* and S. A. Johnson, *Dalhousie University*

Background:

The results of several previous studies of memory in individuals with Autism Spectrum Disorder (ASD) indicate deficits in relational semantic processing and decreased spontaneous use of mnemonic strategies (Gaigg et al., 2008) relative to individuals without ASD. However, when additional external supports are provided at test, individuals with ASD perform more similarly to their typically developing peers, a finding that led Bowler et al. (1997) to develop the Task Support Hypothesis of memory in ASD. The California Verbal Learning Test (CVLT) is a widely used neuropsychological measure of verbal learning and memory that also evaluates the use of strategies, which are thought to reflect executive functioning. To date, there have been no reported studies using the children's version of the CVLT to examine learning and memory in youth with ASD.

Objectives:

We examined learning and memory, as measured by the California Verbal Learning Test, Children's Edition (CVLT-C), in children and adolescents with high-functioning ASD. We were particularly interested in variables pertaining to learning strategies.

Methods:

Participants included 14 children and adolescents with ASD and 14 controls, matched for age, IQ and gender. Estimated IQ was measured using the Wechsler Abbreviated Scale of Intelligence. The CVLT-C is a list-learning task that involves five repetitions of a list of 15 words that includes 3 categories of items (clothes, toys and fruits). Immediate recall, delayed recall, and recognition of the words are assessed. We compared overall recall (List A Trials 1-5 Total, max score = 75), semantic and serial cluster ratios, recall consistency, total perseverations and total intrusions between ASD and control groups. We also examined relationships between CVLT-C performance and estimated IQ and age.

Results:

The ASD and control groups did not significantly differ on measures of semantic and serial cluster ratios, recall consistency, total perseverations, or total intrusions. There was a near significant difference ($p = .07$) for overall recall, with the ASD group recalling fewer items in total (mean = 47.2, SD = 10.8) than controls (mean = 55.3, SD = 11.6). In the ASD group, there was a significant positive correlation between estimated IQ and percent recall consistency ($r = .79$, $p < .01$) and a significant negative correlation between estimated IQ and total intrusions ($r = -.54$, $p < .05$). There were no relationships between IQ and CVLT-C performance for the control group or between age and CVLT-C performance for the ASD group. However, there was a significant negative correlation between age and serial cluster ratio scores for the control group ($r = -.64$, $p < .05$).

Conclusions:

Although these results suggest that individuals with ASD experience some overall deficits in learning and memory, there was no evidence of differences in strategy use. Interestingly, within the ASD group, individuals with a higher IQ showed higher recall consistency and fewer intrusions, suggesting a more systematic approach to the task. Findings will be discussed within the context of current theories of memory dysfunction in ASD, including the Task Support Hypothesis.

120.129 129 Central Coherence in the Broader Autism Phenotype. S. E. Griffiths*[1], J. Parr[2], S. Wallace[1], K. Wittemeyer[1], H. L. Hayward[3] and A. Bailey[1], (1)*University of Oxford*, (2)*Great Ormond Street Hospital*, (3)*Unviversity of Oxford*

Background:

Relatives of individuals with Autism Spectrum Disorders (ASD) with the Broader Autism Phenotype (BAP) show similar but milder cognitive and behavioural difficulties. The family history interview (FHI) is a measure of the BAP, and is conducted on the subject (FHI-S), and with an informant (the subject's spouse or parent) about the subject (FHI-I). We previously reported significant correlations between social difficulties as measured by the FHI and cognitive

performance on Theory of Mind tasks (White et al., IMFAR 2008). Evidence that weak central coherence (CC) is also a part of the BAP is less striking, but has been reported, particularly in fathers, using tests such as the Embedded Figures Task (EFT) and Block Design (BD) (Bölte & Poustka, 2006; Happé et al., 2001; Baron-Cohen & Hammer, 1997). In the general population, males tend to perform better than females on both BD (Lynn & Mulhern, 1991) and the EFT (Witkin et al., 1971). It remains unclear, however, as to whether those relatives with higher total scores on the FHI show evidence of weak CC on the EFT and BD tasks.

Objectives: (1) To identify whether gender differences in CC task performance (Block Design; Embedded Figures Task) reported in the normal population extend to relatives of people with ASD. (2) To assess whether weak central coherence correlates with FHI scores, establishing whether this cognitive function can be related to observations of the BAP.

Methods: One hundred and fourteen parents and siblings from the International Molecular Genetics of Autism Consortium (IMGSAC) collection of multiplex families were assessed. FHI-S and FHI-I were conducted in participants' homes, however only the FHI-I was used in analysis as its test-retest reliability tends to be higher (Bolton, 1994). The EFT and the Block Design task were administered at a later date with other cognitive tests. For the EFT, participants were given 60 seconds to find the embedded figure then trace it with a stylus. BD was scored as part of the WASI IQ and t-scores were obtained.

Results: EFT mean solution time and BD t-scores were strongly correlated ($p<.001$). Contrary to our hypothesis of poorer performance by women on CC measures, there were no significant differences between the performance of male and female relatives of individuals with ASD on either test of CC. Lastly, there was no correlation between either the EFT or BD and the total score from the FHI-I.

Conclusions: Female relatives of people with ASD do not show the usual decreased performance in CC tasks relative to males, which may suggest an underlying difference in the way they process visual information compared with females in the population. The failure to find correlations between the FHI-I and CC task performance suggests that this aspect of cognition may not be directly related to aspects of the BAP, or that these behavioural and cognitive measures are independent.

120.130 130 The Pittsburgh Inference Test (PIT): a Pilot Study Evaluating a Measure of Discourse Processing in Individuals with High-Functioning Autism. K. E. Bodner*[1], N. J. Minshew[1] and D. L. Williams[2], (1)*University of Pittsburgh School of Medicine*, (2)*Duquesne University*

Background: Making inferences requires the integration of linguistic and social information, a process that occurs automatically in individuals with typical development. In autism, inference making has been found to be impaired even in relatively able individuals (Dennis, Lazenby, & Lockyer, *JADD,* 2001; Happé, *JADD*, 1994; Mason et al., *Neuropsychologia*, 2008). There are few measures that evaluate this aspect of discourse processing in individuals who speak Standard American English.

Objectives: The Pittsburgh Inference Test (PIT) is being developed to assess the ability to make inferences during discourse processing in individuals with ASD. This pilot study evaluated the sensitivity of the PIT at the identification of difficulty with inference making in HFA.

Methods: The PIT consists of 34 short stories of common situations that require inferences about physical events, emotional states, or mental states. A question that requires the participant to make an inference about the situation follows each story. The participant generates unique verbal responses that are recorded verbatim by the examiner. The participant's inferences are classified as correct or incorrect, and further coded as physical, emotional, motivational, or nonsensical. The PIT and the Test of Language Competence – Expanded (TLC-E) were administered to 22 adults with HFA (16-40 years; mean = 25.6 years) and 19 adults with TD (16–42 years; mean = 28.1 years), group-matched for age [$t(39)=-1.57$, $p=.12$] and IQ [FSIQ $t(39)=-1.54$, $p=.13$; VIQ $t(39)=-1.69$, $p=.10$; PIQ $t(39)=-.40$, $p=.69$]. Autism diagnosis was determined with the ADOS, ADI, and clinical impression. All participants attained Full Scale IQ's ³ 97. The TLC-E is a formal measure consisting of four subtests that samples metalinguistic abilities. If the PIT and the TLC-E measure related underlying cognitive and linguistic constructs, correlations between these

measures would be expected. However, the PIT may be more sensitive to difficulties in discourse processing because of the nature of the tasks.

Results: A repeated measures ANOVA indicated that the HFA participants performed worse than TD participants on the PIT, with significantly fewer correct responses on the three types of items [F(1, 39)=4.70, p=.04]. Post hoc analysis indicated that the autism group had the most difficulty with items requiring inferences about emotional states [t(39)= -2.04, p=.05]. The correct responses for the HFA group for the emotional states items were moderately to strong correlated with performance on 3 of the 4 subtests of the TLC-E; correct responses for the HFA group on the motivational states were correlated with performance on the "Making Inferences" subtest of the TLC-E. HFA participants were more likely to provide irrational and nonsensical responses to items on the PIT in comparison to TD participants [t(39)=2.62, p=.01].

Conclusions: The PIT identified impaired performance in HFA in making inferences, particularly in ascertaining emotional states. Analysis of the data is being used to make further refinements in this tool that is intended to be used for evaluating discourse processing in high-functioning individuals with autism.

120.131 131 Where Autistics Excel: Compiling An Inventory of Autistic Cognitive Strengths. M. Dawson* and L. Mottron, *Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*

Background: Until recently, there has been little interest in autistic cognitive strengths. Instead, autistic strengths revealed through comparisons between the performance of autistic and nonautistic individuals on various tasks have been largely reported or interpreted as evidence for autistic cognitive deficits (Baron-Cohen, 2005; Gernsbacher et al., 2006; Mottron et al., 2008). Also, there is currently no compilation of empirically documented autistic cognitive strengths as reported in the existing literature. Accordingly, little is known about the full range and quantity of autistic cognitive strengths or the variety and number of autistic individuals in which these strengths have been found.

Objectives: Our aim was to further understanding of cognitive strengths in the autistic population by identifying, quantifying and characterizing existing studies reporting these strengths.

Methods: We located and characterized papers published in peer-reviewed journals which reported autistic cognitive strengths. In order to be included, studies had to compare the performance of autistics to the performance of nonautistics on a task, and autistics had to be reported to perform better than their controls on the task. Studies specific to autistic savants and hyperlexics were excluded, as were probable but unclear reports of autistic strengths, and accidental findings arising from matching strategies. Autistic cognitive strengths originally reported and/or interpreted as deficits were included.

Results: In total, 52 distinct types of autistic cognitive strengths were found, reported in 71 papers (12 reporting two or more strength types) spanning from the 1970s to the present. Only 13 papers published prior to 2000 reported strengths, but at least five papers reporting strengths have been published every year starting in 2000, with the highest number per year in 2008 (N=13). Twelve of the 52 strength types were reported in at least two, and up to 10, papers, with the most replicated finding being superior performance in embedded figures tasks. While most strengths (N=36) were found via tasks using nonsocial information, several strengths involving social information (N=8) and language (N=7) were reported. Sample size for autistic groups ranged from 3 to 40, with a mean of 16, while mean age of autistic participants within samples ranged from 2 to 39 years. Total number of autistics, encompassing 81 different samples, was 1351, of whom 885 had the specific diagnosis of autism, while 130 were diagnosed with Asperger syndrome, and 336 were in the general "ASD" category. Of the 71 papers, 25 included autistic individuals judged to be intellectually disabled according to commonly used instruments, and 29 reported or interpreted one or more findings of autistic cognitive strengths as one or more deficits.

Conclusions: Numerous distinct autistic cognitive strengths, some of them highly replicated, in a wide range of areas, and displayed by a large number and great variety of autistic individuals, have been reported in the literature. Failing to acknowledge the importance of autistic cognitive strengths may impede efforts to understand autistic differences and assist autistic individuals. We recommend more consistent and transparent

reporting and interpretation of autistic cognitive strengths and more attention to their importance.

120.132 132 The Assessment of Cognitive Trait and Thinking Process in ASD using Ambiguous Figure: (2)Developmental Change of Cognition and Emotional Regulation by Aging. M. Myogan*[1], H. Uchida[2] and M. Tsujii[3], (1)*Tokai Gakuin university*, (2)*University of East Asia*, (3)*Osaka-Hamamatsu Joint Center for Child Mental Development*

Background: The people with Autistic Spectrum Disorder(ASD) develop several abilities by Aging. The authors notice development of ASD'S social cognition and emotional regulation need for adjustment. The authors investigate development of the ability(social cognition and emotional regulation) by Aging. Objectives: The authors investigate ASD'S social cognition and emotional regulation from pupil to adult. The authors classify 4 groups (The lower grade group, the upper grade group, adolescence group, Adult group). Methods: The investigation are administered to 55(48mail and 7 female; 13.67±4.94years) children and adults with ASD diagnosed by child psychiatrist. Most of the ASD subjects are members of "Asperger Society Japan". The authors used Rorschach's inkblot-test as the ambiguous figure in Assessment.Group structure is as follow.; The lower grade group(n=9;7.44±0.73years), the upper grade group(n=12;10.33±1.15years), adolescence group((n=11;14.91±1.51years), Adult group(n=11;20.91±2.59years). Results: About development of cognition, popular response that means common sense is increasing by Aging. Form level that means realty testing is also in rising too. About development of emotional regulation, C response that means immature emotional regulation is decreasing, and FC response that means mature emotional regulation is increasing by Aging.

Conclusions: About development of cognition, ASD group learn the ability of social cognition (common sense and realty testing) by Aging. About development of emotional regulation, ASD group immature emotional regulation is decreasing, and FC response that means mature emotional regulation is increasing by Aging.The authors verify that the people with ASD develop ability of social cognition and emotional regulation over having some handicap, again.

120.133 133 The Assessment of Cognitive Trait and Thinking Process in ASD Using Ambiguous Figure: (1)the Comparison with Schizophrenia. M. Myogan*[1], H. Uchida[2] and M. Tsujii[3], (1)*Tokai Gakuin university*, (2)*University of East Asia*, (3)*Osaka-Hamamatsu Joint Center for Child Mental Development*

Background: It has been big problem that the difference between Autistic Spectrum Disorder(ASD) and schizophrenia. That is, some of patients with ASD are look like schizophrenia patients, disturbance of interpersonal relationship, delusion and so on. Objectives: The authors have explored the difference of cognitive traits or thinking process between ASD and schizophrenia. Methods: The investigation are administered to 34(28mail and 6 femail;17.03±3.38years)adolescents and adults with ASD diagnosed by child psychiatrist, and 39 Schizophrenia patients(22mail and 17femail; 22.46±3.87years).Most of the ASD subjects are members of "Asperger Society Japan". The authors used Rorschach's inkblot-test as the ambiguous figure in Assessment. Results: The both group fail in the combination of response. The authors classify failure of combination in two stages. First stage is only "loss of distance(fabulized combination)"; Second stage is not only "loss of distance" but also "Increase of distance"(Confabulation). As a result, schizophrenia group shows Confabulation, But ASD group don't come to the stage of Confabulation. Conclusions: The differences of cognitive traits or thinking process between ASD and schizophrenia are as follows. The ASD's cognitive traits are the weak drive for central coherence because their cognition is gravitated toward detail parts. On the hand, The Schizopherenia's cognitive traits aren't only weak drive for central coherence but also thinking disturbance that too little regard for the reality, and carry too much associative elaboration.

120.134 134 Autoimmune Disorders in Probands and First-Degree Relatives of the Simons Simplex Collection Data. E. Fombonne*[1], R. Maxim[2], M. Steiman[3] and A. Whitaker[4], (1)*McGill University*, (2)*Saint Louis University*, (3)*Montreal Children's Hospital*, (4)*Columbia University Medical Center*

Background: Hypotheses have been raised about an autoimmune model of autism. Some epidemiological data suggest increased rates of autoimmune disorders in first-degree relatives of subjects with autism spectrum disorders (ASD). Regression in ASD has also been postulated to reflect autoimmune dysfunction.

Objectives: To evaluate the lifetime prevalence of autoimmune disorders in ASD probands and in their first-degree relatives, and to compare it to that in the general population; 2. To determine if

phenotypic differences in the ASD probands were associated with the presence or absence of autoimmune disorders in either the proband or his/her first-degree relatives.

Methods: The sample consisted of 414 probands (mean age: 9.5 years; SD = 3.2 – 86.7% male) with ASD (65.7% Autistic Disorder; 21.7% PDD-NOS; 12.6% Asperger's Disorder) collected as part of the Simons Foundation funded genetic study of simplex families. Data regarding the lifetime occurrence of 14 specific autoimmune disorders were collected for the proband, parents, full siblings, and other more distant relatives. Probands had a state-of-the-art research diagnostic evaluation.

Results: Thirty-nine probands (9.4%) had an autoimmune disorder (asthma: 7.0%; lupus: .2%; hypothyroidism: .2%; psoriasis: .5%; celiac disease: .2%; other: .5%). Comparisons of the probands with (N = 39) or without (N = 375) any autoimmune disorder showed no statistical difference for diagnosis, age of recognition of first symptoms, age of first single words or of phrase speech, presence/absence of regression, scores for ADI-R and ADOS, standard scores for IQ and Peabody Picture Vocabulary Test (PPVT), standard scores for the Vineland Adaptive Behavior Scale – Second Edition (VABS-II), Repetitive Behavior Scale Revised (RBS-R) mean factor and total scores, Aberrant Behavior Checklist (ABC) factor scores, and Child Behavior Checklist (CBCL) internalizing, externalizing and total T-scores. There were 163 (39.4%) first-degree relatives with at least one autoimmune disorder (juvenile rheumatoid arthritis: .5%; adult rheumatoid arthritis: 1.9%; lupus: .2%; asthma: 19.8%; hyperthyroidism: 1.4%; hypothyroidism: 4.8%; Hashimoto disease: 1.2%; diabetes Type I: 1.0%; diabetes Type II: 3.6%; psoriasis: 4.8%; celiac disease: .5%; inflammatory bowel disorder: 5.6%; multiple sclerosis: .2%; other: 3.1%). Comparisons of the subgroup of probands with first-degree relatives with (N = 163) or without (N = 251) any autoimmune disorder showed no statistical difference for diagnosis, age of recognition of first symptoms, age of first single words or of phrase speech, presence/absence of regression, standard scores for IQ, VABS-II, PPVT, the RBS-R mean factor and total scores, the ABC factor scores, and the CBCL internalizing, externalizing and total T-scores. Significant differences were found for the social and repetitive ADI-R subscores, and for the socio-communicative and repetitive ADOS scores. These differences were of small magnitude, and were inconsistent in direction and across measures. Comparisons of prevalence rates of autoimmune disorders in this sample with known epidemiological estimates will be presented at the conference.

Conclusions: In cases of ASD that occur sporadically, the presence of autoimmune disorders in the proband or in first-degree relatives was not associated with identifiable variations of the phenotype. Additional studies on autism multiplex families could further evaluate the possible association between autoimmune disorders and ASD.

120.135 135 Expression of the Broad Autism Phenotype in First Degree Relatives from the Simons Simplex Collection. S. U. Peters*[1], R. P. Goin-Kochel[1], R. Hundley[2], Z. Warren[3] and J. N. Constantino[4], (1)*Baylor College of Medicine*, (2)*Children's Hospital*, (3)*Vanderbilt University*, (4)*Washington University School of Medicine*

Background: In order to better understand the biological pathways that contribute to aspects of autism, researchers are examining the milder expression of underlying genetic liability for autism that is manifest in non-autistic relatives, defined as the Broad Autism Phenotype (BAP). There has been some evidence of the BAP in parents and siblings from simplex and multiplex autism families.

Objectives: To extend the existing research by examining differences in measurement of the BAP across multiple instruments and across informants, and the degree to which parental scores predict sibling scores.

Methods: Data were collected via the Simons Simplex Collection (SSC). The SSC is a large, multi-site study that utilizes rigorous phenotyping procedures to study families in which one child (aged 4 to 17) has been diagnosed with an Autism Spectrum Disorder (ASD) but neither parent nor any sibling has been determined to be on the autism spectrum. To assess the BAP, parents completed the Broad Autism Phenotype Questionnaire (BAPQ) about themselves and the Social Responsiveness Scale: Adult Research Version (SRS:ARV) about their partners. In families where one member had an elevated SRS:ARV score (above 70), the Family History Interview Interviewer Impressions were also

completed. Families were excluded if scores on both instruments were elevated. Parents also completed the Social Responsiveness Scale on unaffected siblings (the sibling closest in age to the proband).

Results: 787 parents completed the BAPQ, and 844 parents completed the SRS:ARV. SRS scores were attained for 385 siblings. On the BAPQ, fathers had elevated scores when compared to mothers for Aloof Personality ($p<.001$), Pragmatic Language Deficits ($p<.001$), Rigid Personality ($p<.001$), and Total Score ($p<.001$). Relative to published norms, 278 parents (35%) exceeded BAPQ self-report cutoff scores for Aloof Personality; 210 parents (27%) exceeded cutoffs for Pragmatic Language deficits; 340 parents (43%) exceeded cutoffs for Rigid Personality, and 195 parents (25%) exceeded cutoffs for the total score, indicating that they had multiple features of the BAP. SRS:ARV mean scores were not elevated in comparison to an epidemiologic (previously published) reference sample, and there were no differences between mothers and fathers for overall mean scores. Correlations between the subscales of the BAPQ and the SRS:ARV were significant ($p<.001$), but weak (i.e. $r<.50$). Sibling mean SRS scores were also not elevated. Maternal scores on the SRS and the BAPQ were more strongly correlated with sibling SRS scores compared to paternal scores on either instrument, though correlations were also weak ($r=.26$ or less).

Conclusions: Results regarding the presence/absence of traits related to the BAP differed depending upon the method and instrument that was utilized to assess the BAP. Importantly, the results revealed that the two commonly used self- and informant- report instruments are weakly correlated and may be assessing different constructs. The SRS:ARV allows one to control for total severity of autistic impairment, while the BAPQ assess constructs that the SRS:ARV does not measure. While these results assist in defining intermediate phenotypes and informing models of genetic transmission in simplex families, resolving differences in measurement of the BAP will be important for future studies.

120.136 136 Representing Behavioral Phenotypic Heterogeneity within Autism Spectrum Disorders (ASD): Questions and Answers from the Simons Simplex Collection.

C. Lord*[1], L. Harvey[2], E. Petkova[3], S. Qiu[2], J. Tjernagel[2], R. Bernier[4], J. N. Constantino[5], E. H. Cook[6], O. Ousley[7], W. Stone[8], Z. Warren[8], A. Beaudet[9], D. E. Treadwell-Deering[10], B. Peterson[11], A. Whitaker[12], D. H. Ledbetter[7], C. L. Martin[7], E. Hanson[13], C. A. Walsh[14], E. Fombonne[15], M. Steiman[16], D. Geschwind[17], J. Piggot[17], C. W. Brune[6], D. M. Martin[1], S. M. Kanne[18], J. H. Miles[18], E. M. Wijsman[4], J. Sutcliffe[8], R. Maxim[19], A. Klin[20] and L. Quirmbach[20], (1)*University of Michigan*, (2)*University of Michigan Autism & Communication Disorders Center (UMACC)*, (3)*NYU Child Study Center*, (4)*University of Washington*, (5)*Washington University School of Medicine*, (6)*University of Illinois at Chicago*, (7)*Emory University*, (8)*Vanderbilt University*, (9)*Baylor College of Medicine*, (10)*Texas Children's Hosptial, Baylor College of Medicine*, (11)*Columbia University, NYS Psychiatric Institute*, (12)*Columbia University Medical Center*, (13)*Children's Hospital*, (14)*Children's Hospital Boston*, (15)*McGill University*, (16)*Montreal Children's Hospital*, (17)*University of California, Los Angeles*, (18)*University of Missouri*, (19)*Saint Louis University*, (20)*Yale University School of Medicine*

Background: In several studies, clinical diagnoses and/or certainty ratings made by clinicians within a research group have added to the value of standardized diagnostic and cognitive measures in longitudinal predictions for young children with ASD.

Objectives: The objectives of this study were to 1) assess how such clinical judgments, made across a number of tertiary clinical centers for autism, would compare to standardized assessments and 2) whether the clinical judgments would independently contribute to predictions of current impairment.

Methods: The sample consisted of 414 4 to 17 year-old probands with an autism spectrum disorder (clinical diagnoses: 65.7% autism, 21.7% PDD-NOS, 12.6% Asperger's) from 12 North American clinics. All probands met CPEA-STAART criteria for ASD based on the ADI-R and ADOS (Risi et al., 2006). With appropriate IRB approved consents, families were recruited through the Simons Simplex Collection, a genetic and phenotypic repository for families with one child with ASD and, in most cases, at least one typical sibling. Children with severe to profound nonverbal intellectual disability, cerebral palsy, extensive birth complications, Fragile X, or Down syndrome or first/ second degree relatives with ASD were not included. Probands were assessed with the ADI-R, ADOS, a standard hierarchy of cognitive and language tests, and other behavioral and adaptive measures. Extensive

efforts were made to ensure cross-site reliability of administration and scoring of the standardized measures, as well as procedures for making DSM IV diagnoses.

Results: Use of different clinical diagnoses within ASD was highly variable across sites, with some sites diagnosing most or all children with autism and other sites reporting much higher frequencies of PDD-NOS or Asperger, though the means and distributions of standardized scores on the ADI-R, ADOS and cognitive measures were very similar across sites, with a few exceptions. Use of different ASD diagnoses were related to verbal IQ, age of proband and severity of repetitive behaviors, but also reflected comparative composition of the sample within a site (e.g., how an individual proband compared to other children seen at that site). Adaptive scores and IQs for children with diagnoses of Asperger Syndrome were consistently higher than those of children with autism diagnoses; the relationship of PDD-NOS to either of the other diagnoses, adaptive functioning and all other measures was highly variable, as were proportions of children receiving different diagnoses within very similar distributions of standardized scores.

Conclusions: In the past, within-site clinical judgments of subtypes of ASD (autism, PDD-NOS, Asperger) have offered a useful source of information about functioning for young children with spectrum disorders. However, in a multi-site study of older children, such judgments were far less interpretable. Predictable factors could be identified within most sites which related to different clinical diagnoses, however, the particular factor of greatest influence varied considerably across sites, even when a standard battery of instruments was used and procedures were highly similar. Implications for the validity of clinical diagnoses within ASD will be discussed.

120.137 137 Characterization of Restricted and Repetitive Behavior and Interests in Autism Spectrum Disorders within and beyond the ADI-R Using the Simons Simplex Collection. C. W. Brune*[1], E. Hanson[2], J. Piggot[3], O. L. T. Wong[3] and M. Gregas[4], (1)*University of Illinois at Chicago*, (2)*Children's Hospital*, (3)*University of California, Los Angeles*, (4)*Children's Hospital Boston*

Background: Restrictive repetitive behavior and interests (RRB) represent a core domain of autism spectrum disorders (ASDs), which are assessed on the Autism Diagnostic Interview-Revised (ADI-R). Recent analysis identified three factors of RRB on the ADI-R: Insistence on Sameness, Repetitive Motor Behaviors, and Circumscribed Interests (Lam, Bodfish, & Aman, 2008). Similar factors are among the five produced on the Repetitive Behavior Scale-Revised (RBS-R), which was created as an independent measure of the severity of RRB. It is unknown whether the measurement of RRB on these instruments relates, whether they are both useful for characterizing phenotypes, and how their characterizations of RRB relate to common non-core behavior including aggression, anxiety, and hyperactivity.

Objectives: The goals of this study are: 1) to identify the prevalence, severity, and patterns of RRB in a large ASD population, and how these vary by sex, age, cognitive ability, and language use, 2) to investigate the relation between RRB factors derived from the ADI-R and the RBS-R, 3) to test whether RRB as captured by these instruments relates to non-ASD behaviors.

Methods: Individuals participating in the Simons Simplex Collection, a North American multiple site, university-based research study of the genetics of ASDs that includes approximately 420 families with only one child with an ASD, completed an extensive battery of diagnostic measures. All study probands were 4 to 17 years of age and met criteria for a research diagnosis of an ASD (Risi et al., 2006) based on the ADI-R, the Autism Diagnostic Observation Schedule (ADOS), and clinical consensus. Primary ineligibility criteria included a diagnosis of an ASD in the proband's first or second degree relatives or cousins. Approximately 25% of the families in the SSC have one child with an ASD but no other children. Parents completed several measures about their children including the ADI-R, RBS-R, the Child Behavior Checklist (CBCL), and the Aberrant Behavior Checklist (ABC). Descriptive analysis of item level data will show the prevalence and severity of individual behaviors. Independent factor analysis of the RRB items on the ADI-R and all items on RBS-R will be conducted. Correlations between factor scores from each analysis, age, and IQ will be calculated, and factor scores will be compared across language use and sex. A combined analysis of these instruments incorporating age, sex, IQ, and language use will be produced. The derived measures of RRB will be used to assess the

relation between RRB and behavior problems on the CBCL and ABC.

Results: The most prevalent and frequently endorsed aspects of RRB in this sample will be identified. Three sets of RRB factors will be derived in the analyses. The relation between individual factor scores will show whether the ADI-R and RBS-R capture similar components of RRB.

Conclusions: These analyses will be put in context of previous research trying to identify subtypes of RRB which may be useful phenotypes for genetic and treatment studies of ASDs.

120.138 138 Symptoms of Psychiatric Comorbidity in Children and Adolescents with Autism Spectrum Disorders: An Examination of the Child Behavior Checklist from the Simons Simplex Collection Database. O. Ousley*[1], E. H. Cook[2] and D. E. Treadwell-Deering[3], (1)*Emory University*, (2)*University of Illinois at Chicago*, (3)*Texas Children's Hosptial, Baylor College of Medicine*

Background: Children and adolescents with autism spectrum disorder (ASD) frequently exhibit comorbid psychiatric symptoms, and according to a recent population-derived study of 112 children with ASD, 70% meet diagnostic criteria for at least one comorbid disorder, and 41% meet criteria for two or more disorders, such as social anxiety disorder, ADHD, and oppositional defiant disorder (Simonoff et al., 2008). The individual factors which may be associated with an increased risk of comorbid disorders in ASD have not yet been identified.

Objectives: In this study, we will characterize the psychiatric and behavioral profiles of a large sample of children with ASD who participated in the Simons Simplex Collection (SSC), a North American multiple-site, university-based research study that includes 420 families with only one child with an ASD. We will also examine how age, verbal ability, and autism severity are related to severity of comorbid symptoms, as evaluated by the Child Behavior Checklist (CBCL), a parent report measure.

Methods: We will examine data from approximately 420 SSC probands who meet criteria for a research diagnosis of an ASD (Risi et al., 2006), based on the Autism Diagnostic Interview-Revised (ADI-R), the Autism Diagnostic Observation Schedule (ADOS), and clinical consensus. We will identify the percentage of probands who exhibit elevated internalizing and externalizing symptom scores and elevated DSM-IV-related symptom scores, and will examine how individual factors (e.g., age, verbal ability, and autism severity) are associated with the level of comorbid symptom presentation. Verbal mental age obtained from the Mullen Scales of Early Learning or the Differential Ability Scales (DAS-II), an ADOS-derived autism severity index (Gotham et al., in press), and the ADI-R domain scores will be used in the analyses.

Results: Preliminary data analysis of 85 probands (Mean Age = 118.86 months, SD = 34.51) indicates that 30.6% and 20.0% of the probands have elevated CBCL Internalizing and Externalizing behavior scores. The CBCL-DSM-IV-related subscales are also elevated in a subset of probands: Affective problems, 28.2%; Anxiety problems, 35.3; Somatic problems, 8.2%; ADHD problems, 26.2%; Oppositional Defiant problems, 27.1%; and Conduct problems, 15.3%. Correlation analysis shows that higher verbal mental age is associated with higher Internalizing and Externalizing problems ($r = .48$, $p < .001$, and $r = .32$, $p < .05$, respectively) and with higher DSM-IV-related subscale scores (except for the ADHD problems score). Correlation analysis also reveals that chronological age and autism severity is generally not associated with comorbid symptom scores.

Conclusions: In this study, up to 30% of children and adolescents with ASD exhibit clinically significant comorbid psychiatric symptoms, as evaluated by the CBCL. An examination of individual factors shows that increased severity of comorbid symptoms is associated with higher levels of verbal ability, but that severity of comorbid symptoms is not associated with age and autism severity. Our results provide some evidence that comorbid symptoms may reflect the presence of distinct psychiatric disorders, unrelated to the presence of an ASD; however, future studies are needed to examine the onset and the developmental trajectory of comorbid symptom presentation in children with ASD.

120.139 139 Relationship Between Adapitve Functioning, IQ, and Symptom Severity in Individuals with ASD: The Simons Simplex Collection. A. J. Gerber*[1], S. M. Kanne[2], L. Quirmbach[3], M. Algermissen[1], P. D. LaVesser[4] and C. A. Saulnier[3], (1)*Columbia University / New York State Psychiatric*

Institute, (2)*University of Missouri*, (3)*Yale University School of Medicine*, (4)*Washington University*

Background: Research has indicated a weak relationship between ability (measured by Vineland scores) and disability (measured by ADOS scores) among high functioning individuals with ASD; despite having a Verbal IQ > 70, these individuals demonstrated significant vulnerabilities in their adaptive functioning (Klin, Saulnier, Sparrow et al., 2007).

Objectives: The purpose of the current study is to examine the relationship between adaptive functioning and autism symptomatology in a sample of 334 individuals with ASD ages 4 to 16. These individuals participated in the Simons Simplex Collection (SSC), a North American multiple site, university-based research study that includes approximately 420 families with only one child with an ASD.

Methods: Participants included 334 individuals with ASD (218 with autism, 76 with PDD-NOS, and 40 with Asperger Syndrome), ages 4 to 16 (mean age = 9.0 years). Correlation analyses were completed between Vineland, IQ (i.e., Mullen, DAS-II, WISC-IV and WASI), ADI-R scales, and ADOS severity scores. ADOS severity scores were based on creating a normal curve for each ADOS module and then determining each individual's level of severity depending on where they fell along the respective curve for that module, with scores ranging between 1 and 10.

Results: Vineland results were as follows (mean): Composite = 78.6, Communication = 82.7, Social = 75.4, and Daily Living = 83. Results of IQ measures were (mean): Full Scale IQ = 93.1, Verbal IQ = 89.9, Nonverbal IQ = 96.6. The mean ADOS severity score was 7.42. Strong positive relationships were found between Full Scale IQ and Vineland subscales (Communication r = .47*;* Socialization r = .36; Daily Living Skills r = .44), suggesting that individuals with higher IQ scores have more advanced adaptive skills. Vineland Communication and Socialization subscales were weakly associated with ADOS severity scores (Communication r = -.13*;* Socialization r = -.15) but more strongly with ADI diagnostic scores (ranging from r = -.23 to r = -.35). Conversely, Vineland Daily Living Skills were more strongly associated with ADOS severity scores (r = -.28), but less so with ADI-R diagnostic scores (r = -.19 and r = -.21). ADI-R repetitive behavior scales were not significant with Vineland scores. Stronger negative correlations were found between age and Vineland Communication (r = -.36) and Socialization scores (r = -.26) than for Daily Living (r = -.15).

Conclusions: As in prior research, intellectual functioning predicted higher levels of adaptive ability. Adaptive communication and social skills were only marginally associated with current disability as assessed from direct observation of the individual (ADOS), but more strongly related to parent report of past communication and social interaction difficulties (diagnostic ADI-R). These results suggest that for communicative and social, but not daily living skills, past symptom severity as reported by a parent is a stronger predictor of later adaptive problems than current symptomatology (as assessed by an independent observer), and that the acquisition of these skills does not keep pace with age expectations, despite level of cognitive functioning.

120.140 140 Characterisation of Cognitive Profiles in Autism Spectrum Disorder Using the Simons Simplex Collection. J. Piggot*[1], R. Loftin[2] and L. Guy[3], (1)*University of California, Los Angeles*, (2)*University of Illinois at Chicago*, (3)*Marcus Autism Center, Emory University School of Medicine*

Background: The Simons Simplex Collection (SSC) is an ongoing study that aims to collect data on a total of 2000 families with one individual affected by an Autism Spectrum Disorder (ASD), otherwise known as simplex families. The SSC differs from other studies of ASD in that the focus is the collection of a sample enriched for denovo mutations, including deletions and duplications of genetic material. The relationship between cognitive profiles and ASD symptomatology has previously been described in ASD research in multiplex families; whereas similar investigation has never been explored in simplex families.

Objectives: This study aims to explore for phenotypic areas of interest for the genetic study of this simplex sample. Specifically, the relationship between the cognitive profiles and autism symptomatology of individuals with ASD in the SSC.

Methods: The proposed analysis aims to examine cognitive profiles and their relationship to symptomatology in a large sample of children with ASD who participated in the SSC, a North American multiple site, university-based research study that includes approximately 420 families with only one child with an ASD. The primary ineligibility criteria included severe to profound intellectual disability, severe cerebral palsy, extensive birth complications, Fragile X, or Down Syndrome in the proband, and a diagnosis of an

ASD in the proband's first or second degree relatives or cousins. Approximately 25% of the families in the SSC had one child with an ASD but no other children.
Written consent and assent, as appropriate, was obtained separately for each family member prior to study enrollment. All family members enrolled in the study provided DNA samples and completed a standard assessment battery which included a series of parent interviews, a medical history interview, direct assessment of the proband, and completion of behavioral/cognitive questionnaires relevant to each family member. All study probands were 4 -17 years of age and met criteria for a research diagnosis of an ASD, based on the Autism Diagnostic Interview-Revised (ADI-R), the Autism Diagnostic Observation Schedule (ADOS), and clinical consensus.
Data from each site was merged into a common relational database designed by Prometheus Research, LLC, and DNA samples were stored at the Rutgers University Cell and DNA Repository.

Results: This study will present the results of the analysis of the above data. Autism symptomatology measured using the ADI-R and ADOS will be related to the cognitive profiles of children expressing the ASD phenotype. Beyond the study of measured variables; exploratory factor and cluster analyses will be undertaken to look at the relationships of the cognitive "factors" (dimensions); and cognitive "cluster" (subtypes); with social communication impairment, language and repetitive behaviors. The relationship of the severity of cognitive impairments, focusing on language impairment and milestones, will also be explored.

Conclusions: Findings from this study will provide evidence for any potential association between cognitive profile and phenotypic characteristics in ASD population. The results of this study along of the results found by other SSC phenotype committee will provide insight into understanding the pattern of autistic characteristics presented in affected children of similar genetic background.

120.141 141 Rey-Osterrieth Complex Figure Performance in High-Functioning Individuals with ASD: An Update. K. D. Tsatsanis*[1], I. L. J. Noens[2], C. L. Illmann[3], D. L. Pauls[3], F. R. Volkmar[4], R. T. Schultz[5] and A. Klin[4], (1)*Yale Child Study Center*, (2)*Katholieke Universiteit Leuven*, (3)*Massachusetts General Hospital*, (4)*Yale University School of Medicine*, (5)*Children's Hospital of Philadelphia and the University of Pennsylvania*

Background: Children and adults with an Autism Spectrum Disorder (ASD) are reported to show a cognitive bias toward a part-oriented processing style. Deficits in some executive processes are also found. The widely used Rey-Osterrieth Complex Figure Test (ROCF) provides a measure by which to investigate the effects of both processing style and organizational strategies when encoding and subsequently recalling a novel and complex stimulus.
Objectives: This study seeks to examine the ROCF performance of children and adults with ASD with comparisons to typically developing children and adults and other clinical groups (children with TS, OCD, and/or ADHD).
Methods: The ROCF was administered to 170 high functioning individuals (Full Scale, Verbal, and Performance IQ scores of 70 or above; age range 6:0 – 42:6 years). The sample consisted of three subgroups: individuals with ASD (n=50), typically developing individuals (n=49), and individuals with TS, OCD, and/or ADHD (n=71). The drawings were scored with two scoring systems: the Developmental Scoring System (DSS; Bernstein & Waber, 1996) and the Boston Qualitative Scoring System (BQSS; Stern et al., 1999). Quantitative analyses of performance examined differences in processing style and visuo-spatial planning/organization, and the differential impact on immediate and later recall.
Results: At IMFAR 2008, preliminary results of this study were reported (for children between 8 and 14 years of age only). We have now analyzed DSS data for all age groups; at IMFAR 2009, we report on the BQSS data as well. There is a very robust finding when comparing the DSS data of the three groups (ASD, NC, CC): individuals with ASD process the ROCF in a more part-oriented way than the TD group. This is most evident in the older age group (14:0 – 42:6 years), where part-oriented processing also discriminates the ASD group from the CC group. There are no significant differences between the three groups with respect to the organization of the figure. Additionally, whereas organization and style of processing are strongly correlated in the TD (r=.609) and CC (r=.562) groups, this relationship is not significant in the ASD group (r=.290). Regression analyses indicate that a model using the variables age, IQ, organization and style as predictors accounts for a significant proportion of the variance in recall outcome for the TD and ASD groups. Although both are correlated with recall scores, the part-r values

indicate a significant unique contribution of style for the TD group and organization for the ASD group.
Conclusions: The results of this study indicate that individuals with ASD are distinct from TD and CC groups in the following ways when processing novel complex information: (1) the approach is more part-oriented; (2) processing style is somewhat independent of organization and (3) there does not appear to be a shift to a more configurational approach with age. Additionally, although both organization and style of processing are associated with recall, a more configurational style appears to be a significant unique variable for the NC group whereas organization may be especially relevant to recall for individuals with ASD.

Invited Educational Symposium Program
121 Psychiatric Comorbidities and Treatment

Speakers: J. A. Hellings[1] T. Owley[2] B. Handen[3] (1)*University of Kansas Medical Center*, (2)*University of Illinois at Chicago*, (3)*Univ of Pittsburgh*

121.00 Diagnosis and Treatment of ADHD Symptoms In Autism. B. Handen*, *Univ of Pittsburgh*

While DSM-IV (APA, 2000) specifically excludes a comorbid diagnosis of ADHD for children diagnosed with a Pervasive Developmental Disorder, a significant number of children with PDD display symptoms of overactivity, impulsivity, and inattention. In fact, in a recent survey of behavioral and emotional problems in children and adolescents with PDD, the most frequently endorsed symptoms were those related to ADHD (Lecavalier, 2006). Surveys of psychopharmacology prescribing rates have found that over 10% of children with PDD are prescribed medication to treat the constellation of ADHD symptoms (Aman et al., 2003). This presentation will first review our current knowledge regarding the rate of ADHD symptoms in the PDD population and how frequently clinicians appear to be targeting these symptoms for treatment. Second, diagnostic considerations will be discussed, with a focus on differentiating between symptoms suggestive of a comorbid diagnosis of ADHD and the core features of PDD. Third, an overview of the literature will be provided on pharmacologic treatment of ADHD symptoms in this population, including the use of stimulants, atomoxetine, alpha-two agonists, and atypical antipsychotics. Finally, research on psychosocial treatments of ADHD symptoms in PDD will be reviewed, with an emphasis on recent data regarding the use of parent training in children with PDD.

121.01 Anxiety and Obsessive Compulsive Disorder Issues in Autism Spectrum Disorders. T. Owley*, *University of Illinois at Chicago*

Symptoms similar to those seen in Obsessive Compulsive Disorder (OCD) are often also seen in Autistic Spectrum Disorders (ASD). It is not uncommon to see those with ASD to exhibit obsessions, compulsions, rigidity in thinking and behavior, insistence on sameness, and ritualistic behaviors. There is evidence from genetics, neuroimaging, and the response to specific pharmacological agents to suggest that there are significant connections to be made between these two diagnostic arenas. The degree to which these symptoms are identifiable or considered distinct has ramifications for diagnosis and treatment, as well as implications for future candidate gene studies.

In this presentation, the speaker will focus in particular on the serotonin system as a basis for many of these commonalities. The evidence for hyperserotonemia in ASD was established in the early 1960s and has been replicated many times since that time. In addition, tryptophan depletion studies and gene studies have both implicated serotonin as involved in ASD. There is evidence for an increased incidence of OCD in relatives of those affected with ASD. In both ASD and OCD, there have been findings of positive relief of symptoms with the use of selective serotonin reuptake inhibitors.

The speaker will present pharmacogenetic data from a recent study of escitalopram in ASD. This was a study of children and adolescents receiving the drug, with the Aberrant Behavior Checklist, Community Version, as the primary outcome measure. This genotype-blind, prospective pharmacogenetic study found the following differences in response as a function of 5-HTTLPR genotype: 1) The group of subjects with higher expressing 5-HTTLPR genotypes had a better response to pharmacotherapy than subjects with a low expressing genotype group and 2) there was a difference in the final dose by genotype groupings, with the lowest expressing genotype

group having a lower final dose when compared with higher expressing genotype groups.

Finally, there will be a discussion of emerging concepts regarding differentiation and treatment of symptoms of OCD and ASD. Future directions for research will be reviewed and examined.

121.02 Mood Disorders Comorbid with Autism Spectrum Disorders. J. A. Hellings*, *University of Kansas Medical Center*

Mood disorders in individuals with Autism Spectrum Disorders (ASD) are often associated with aggression and self-injury (Hellings, 1999). Bipolar disorders are often missed or are misdiagnosed and treated as Depressive Disorders, as occurs in the general population. An Expert Consensus Guidelines (2000) review found that valproic acid, other mood stabilizers and antipsychotics are most commonly prescribed by experts treating adults with intellectual and developmental disabilities and behavior problems including aggression. Additionally, treatment response appears significantly slower and side effects greater than in the general population. Studies of the neurobiology of these conditions, including genetics, imaging and treatment responses are urgently needed.

A case study of severe recurrent mania with psychosis will be presented to illustrate diagnostic, treatment and response issues. An overview of clinical presentations, neurobiology and any genetic studies of individuals with ASD and mood disorders will be provided. Diagnostic pitfalls, including missed ADHD, will be included.

Treatment studies, including the negative valproic acid study for aggression in youth with ASD (Hellings et al., 2005) will be reviewed. Risperidone efficacy and side effects in this population will be discussed. Future research directions will be discussed.

Oral Presentations Program
122 Animal Models

122.00 Differential Synaptic Changes in Model Systems of Autism Spectrum Disorders. O. Bozdagi, J. D. Buxbaum*, G. Cai, P. R. Hof, G. Huntley, L. Ospina, T. Sakurai, N. Takahashi and Q. Zhou, *Mount Sinai School of Medicine*

Background: Rare variants associated with high odds ratios are increasingly being found in autism spectrum disorders (ASDs). These rare variants can be studied in model systems, including cell and animal models. We have developed a pipeline for the study of mouse models and are also developing a pipeline for zebrafish models. Currently, we are studying SHANK3 and CYFIP1 as ASD genes in these systems
Objectives: The goal of our study is to make use of animal models to first understand the pathogenesis of ASD associated with specific causal variants and then to attempt interventions in the model systems.
Methods: Mouse knockouts targeting Shank3 and Cyfip1 were developed using standard techniques. In addition, zebafish morphants are being developed as well. The mouse models have been analyzed using biochemical, electrophysiological, and neuropathological approaches.
Results: Loss of one copy of Cyfip1 led to enhancements in long-term depression (LTD) in the hippocampus, without effects on long-term potentiation (LTP). Moreover, LTD in the Cyfip1 heterozygotes was not sensitive to protein synthesis inhibitors, unlike in wild-type animals. Haploinsufficiency of Shank3 also led to synaptic deficits. However, unlike the observations with Cyfip1-heterozygotes, Shank3-heterozygotes showed deficits in LTP as well as presynaptic alterations.
Conclusions: The enhanced LTD and its insensitivity to protein synthesis inhibitors observed Cyfip1-heterozygotes is similar to what observed in mouse models of fragile X syndrome. This is interesting because the fragile X protein directly binds to Cyfip1. The deficits associated with Shank3-haploinsufficiency are different from those observed with Cyfip1-haploinsufficiency consistent with a model in which deficits in multiple independent pathways can lead to ASDs.

122.01 Autism as Synapsopathy: Animal Models Based on Genetic Mutations in Trans-Synaptic Cell Adhesion Molecules. C. M. Powell*[1], M. R. Etherton[1], C. Blaiss[1], K. Tabuchi[2], J. Blundell[1], R. Hammer[1], X. Liu[1] and T. Sudhof[2], (1)*The University of Texas Southwestern Medical Center*, (2)*Stanford Medical School*

Background: A small percentage of patients with autism spectrum disorders carry missense or nonsense mutations in genes encoding neuroligin-3 and -4, which are postsynaptic cell adhesion molecules, and neurexin-1, their presynaptic ligands. In addition, the neurexin-1 binding partners neuroligin 1 and 2 are located on chromosomal regions linked to autism. We have recently characterized mouse models lacking neuroligin 1, 2, or 3 as well as an autism-associated neuroligin 3 point mutation. We describe the behavioral, electrophysiological, and

synaptic phenotypes in these mutant mice. In addition, we are beginning to use pharmacologic approaches to rescue behavioral deficits in these models.

Objectives: To create and characterize a genetically accurate mouse models of autism.

Methods: We have introduced the R451C-substitution in neuroligin-3 into mice by homologous recombination. Neuroligin 1, 2, and 3 knockout mice have been created through traditional methods. All behavioral experiments were performed blind to genotype on 19-22 littermate pairs. A thorough array of behavioral tests relevant to autism and cognitive function, whole cell and extracellular synaptic electrophysiology, electron microscopy, Western blot for synaptic proteins, and immunohistochemistry for synaptic proteins were performed.

Results: R451C-mutant knockin mice showed relatively selective impairment in social approach behavior and increased inhibitory synaptic transmission in cortex, while neuroligin 3 deletion mutants were normal in this regard.

Neuroligin 1 knockout mice showed decreased NMDA-receptor mediated synaptic transmission, a likely cause of their decreased long-term potentiation in area CA1, decreased hippocampus-dependent spatial learning, and increased repetitive behavior as measured by a doubling of time spent grooming. Of relevance to autism, neurexin-1 levels are significantly decreased in these mice. Consistent with a link between repetitive grooming behavior and decreased NMDA receptor-mediated synaptic transmission, the partial NMDA receptor agonist, D-cycloserine, reversed grooming abnormalities. Neuroligin 2 knockout mice revealed a decrease in inhibitory synaptic transmission and concomitant increased anxiety-like behavior.

Conclusions: The neuroligin-3 R451C knockin mice represent the first-published, genetically accurate model of autism not associated with a broader neuropsychiatric syndrome. Furthermore, in agreement with recent findings of decreased cortical excitability in mouse models of Rett syndrome, increased inhibitory synaptic transmission may contribute to human ASDs (Tabuchi et al, *Science*, 2007).

The finding of increased repetitive behaviors and cognitive dysfunction in neuroligin 1 knockout mice may be of relevance to autism since neuroligin 1 is a postsynaptic binding partner of autism-associated neurexin-1 and these mice also have a significant decrease in neurexin protein levels. We have now pharmacologically linked the NMDA receptor dysfunction in these mice to increased repetitive behaviors implicating a potential therapeutic target in these mice.

122.02 Effects of Reduced Reelin Expression and Altered Sex Steroids on Brain Circuitry and Behavior in Mice. F. Keller*[1], F. Biamonte[1], M. Marano[1], E. Romano[2], S. Macrì[2] and G. Laviola[2], (1)*Università Campus Bio-Medico*, (2)*Istituto Superiore di Sanità*

Background:
Reelin is a candidate gene for neurodevelopmental disorders such as autism and schizophrenia. Reelin haploinsufficiency in the heterozygous rl/+ mouse causes behavioral abnormalities soon after birth, consisting of decreased ultrasound vocalizations (USV) emitted by pups upon maternal separation, as well as in adult life, producing behavioral rigidity in a task requiring a change in strategy. At the anatomical level, reelin haploinsufficiency causes a loss of GABAergic inhibitory neurons, e.g. parvalbumin-positive neurons in limbic areas and basal ganglia, and Purkinje cells (PC) in the cerebellum. This PC loss is more evident in male than female mice.
Objectives:
1) To characterize brain circuit abnormalities of heterozygous reeler (rl/+) mice, and their sex-dependency; 2) To unravel the mechanisms of neuronal loss in brain areas that are relevant for autism, like the cerebellum and limbic system, focusing on interactions between decreased reelin levels and sex steroids; 3) To characterize the relationship between circuit alterations and behavioral abnormalities of rl/+ mice, in particular decreased USV.
Methods:
1) Assessment of neuronal numbers with unbiased stereology; 2) Manipulation of brain levels of sex steroids using agonists and antagonists; 3) Measurement of reelin mRNA levels with RT-PCR; 4) Assessment of USV emitted by pups after separation from the mother; 5) Assessment of behavioral flexibility in a strategy-changing task (Intradimensional-Extradimensional Set Shifting Task).
Results:
PC numbers are selectively reduced in rl/+ males

at postnatal day 15, with no parallel loss of their main presynaptic input neurons, i.e. granule cells and inferior olivary neurons. Early postnatal administration of the estrogen receptor (ER) agonist 17β-Estradiol (17βE) in the cisterna magna leads to recovery of PC numbers in male rl/+, but has no effect in female rl/+, or +/+ mice of either sex; conversely, ER antagonists 4-OH-Tamoxifen or ICI 182,780 selectively reduce PC numbers in female +/+ and rl/+, while the same ER antagonists have no effect in male rl/+ or +/+ mice. RT-PCR analysis revealed that 17βE administration restores reelin mRNA levels in rl/+ mice, indicating that transcription of the reelin gene is under 17βE control in the cerebellum. Administration of 17βE in the cisterna magna at P5, in doses leading to recovery of PCs, also leads to an increase of USV of rl/+ mice, in response to maternal separation, as well as a better test performance in the adult rule-shifting task.

Conclusions:

Taken together, these results strongly suggest that reelin and 17βE interact during neurodevelopment to sculpt cerebellar circuitry. This effect may represent a novel model to understand how a genetic mutation interacts with perinatal sex hormones, leading to gender-dependent abnormalities of neural circuits and behavior that persist into adulthood. Furthermore, in conjunction with recent experimental evidence showing that brain levels of 17βE are rapidly modulated by the social context, similar to other classical neuromodulators, our results suggest a novel way of understanding mechanisms by which the environment permanently sculpts neural circuits during brain development. Finally, our data may help to build a neurobiological foundation for the extreme male brain theory of autism.

122.03 The Genetics of Social Behavior in Mice: Implications for Autism Spectrum Disorders. V. J. Bolivar*[1] and R. C. Auerbach[2], (1)*Wadsworth Center, New York State Department of Health*, (2)*School of Public Health, University at Albany*

Background: Varying in presentation and severity of symptoms, autism spectrum disorders (ASD) are likely influenced by a combination of genetic and environmental factors. Despite decades of research and evidence of a strong genetic component, to date little is known about their etiology. As with Huntington's, schizophrenia and Alzheimer's, mouse models may play a critical role in helping us understand the etiology of ASD and develop more effective therapies. Through careful behavioral analyses most of the core characteristics of ASD (i.e., impairments in social interaction, restlessness and distraction, difficulty with language, repetitive and stereotyped motor behaviors) can be modeled in mice. One of the defining characteristics of ASD, impaired social interaction, can be easily studied in mice. Some inbred strains (e.g., BTBR T+ tf/J (BTBR), A/J, BALB/cBy) display lowered sociability compared to others (e.g., C57BL/6J (B6), FVB/NJ (FVB)) and thus are selected for further genetic analysis.

Objectives: Our laboratory is investigating the role of genetics in impaired social behavior in A/J and BTBR inbred strains. The objective of our current research is to examine the role of genetics in sociability in mice. Ultimately, we want to understand the biology of social behavior and how we can develop appropriate therapeutic interventions for ASD.

Methods: We measured sociability through a social approach assay. In one study we examined social behavior in a set of chromosome substitution strains developed by crossing B6 and A/J. The effects of each chromosome from the A/J strain are studied in isolation, while maintaining the remainder of the genetic background as B6. Although these strains do not reveal individual genes, they do implicate the gene set from specific chromosomes, which can then be studied further by microarray and recombinant analyses. We also examined these strains in anxiety and activity assays (open field, zero maze). This way we can separate genetic regions unique to sociability from those related to activity and/or anxiety. Thus, the degree to which activity and anxiety contribute to social behavior is assayed. In another series of studies, we generated a small F2 population between BTBR and FVB strains and examined sociability and neuroanatomy. This study examines both the genetics of social behavior and related neurobiological markers.

Results: The consomic study indicates that a large number of chromosomes are involved in social behavior in mice. Some of these chromosomes are also involved in activity and anxiety-related behaviors. However, a few chromosomes appear to be uniquely involved in social behavior. The behavioral analyses of the F2 mice illustrate a wider range of sociability in this population than in either of the parental strains, as well as, a

small but significant correlation between sociability and corpus callosum size. Additional genetic and neuroanatomical analyses are ongoing.

Conclusions: Inbred strains of mice are an important tool for elucidating the genetics underlying impairments in social interaction. Our studies illustrate that many genetic regions are linked to social behavior in mice. These regions must be studied in more detail to establish specific genes involved in social behavior and ultimately ASD.

122.04 Alterations in the Indirect Basal Ganglia Pathway in An Animal Model of Repetitive Behavior. M. Lewis*, Y. Tanimura, S. Vaziri and D. Khosrowzadeh, *University of Florida*

Background: Although restricted repetitive behaviors are diagnostic for autism and commonly observed in related neurodevelopmental disorders, little is known about specific pathophysiological mechanisms mediating their development or expression. Our lab has employed a deer mouse (*Peromyscus maniculatus*) model that involves spontaneous expression of high rates of motor stereotypies. We have previously shown that these behaviors are associated with alterations in cortico-basal ganglia circuitry. This circuitry includes two key pathways, the direct and indirect, alterations of which have been implicated in other neurological disorders. Results of a prior study from our lab suggested that expression of high levels of repetitive behavior in these mice was associated with reduced activity of the indirect basal ganglia pathway.

Objectives: To confirm and extend our prior study, we assessed whether alterations in basal ganglia indirect pathway function were associated with stereotypy using both biochemical and pharmacological methods.

Methods: We assessed repetitive behavior in deer mice and then measured neuronal metabolic activation in the subthalamic nucleus (STN), a key nucleus of the indirect pathway. Cytochrome oxidase (CO) histochemistry was used to index long-term neuronal activation. In a second set of studies, we altered the activity of the indirect pathway by administration of a selective adenosine$_{2A}$ (A_{2A}) agonist or antagonist to deer mice and assessed its effects on repetitive behavior. A_{2A} receptors are enriched in striatum and expressed on medium spiny GABA cells that make up the indirect pathway.

Results: CO staining in the STN was significantly reduced in high versus low (median split) stereotypy mice. Further, CO staining was significantly negatively correlated with the frequency of stereotypy. Consistent with this finding, a selective A_{2A} agonist reduced repetitive motor behavior in deer mice presumably by increasing the activity of the indirect pathway. Conversely, a selective adenosine$_{2A}$ antagonist induced repetitive behavior in the form of compulsive grooming.

Conclusions: Higher rates of spontaneous repetitive motor behavior were associated with reduced neuronal activation of the indirect basal ganglia pathway. The importance of this pathway in repetitive behavior was strengthened by a reduction of spontaneous stereotypy consequent to activation of adenosine receptors expressed on striatal indirect pathway neurons. Induction of compulsive grooming following blockade of those same receptors provided further support for the importance of the indirect pathway. These findings complement and extend our previous work and support the hypothesis that spontaneous stereotypic behavior in this model is associated with reduced indirect pathway activity. Moreover, adenosine$_{2A}$ receptors may provide a therapeutic target for the treatment of restricted repetitive behavior in autism.

122.05 Behavioral and Neurochemical Characterization of the Serotonin Transporter Gly56Ala Knock-in Mouse. J. Veenstra-VanderWeele*, C. L. Muller, J. Cohen, T. Jessen, B. Thompson, A. M. D. Carneiro, C. B. Zhu, M. D. Carter, H. C. Prasad, J. Sutcliffe and R. D. Blakely, *Vanderbilt University*

Background: Elevated platelet serotonin (5-HT), termed hyperserotonemia, is present in about one-quarter of children with autism. Linkage studies in families containing two or more male children with autism have implicated the chromosome 17q11.2 region containing the serotonin transporter gene (SERT, SLC6A4). Common functional variants in SERT fail to explain the strong linkage signal observed at this locus. In families with male-only probands, rare SERT amino acid variants show an association with autism. The most common of these variants, Gly56Ala, is associated with rigid-compulsive behaviors and sensory aversion. Objectives: In vitro studies (Prasad et al., 2005; Prasad et al., 2009) demonstrated that the 56Ala variant (1) displays increased basal 5-HT transport, (2) exhibits elevated basal phosphorylation, and (3) is

refractory to regulation through PKG and p38 MAPK pathways. To pursue the physiological significance of these findings in vivo, we developed a SERT Gly56Ala knock-in mouse line. Methods: Serotonin levels were measured in whole blood and in brain by high-performance liquid chromatography. Serotonin uptake was measured in platelets and midbrain synaptosomes. Mouse behavior was assessed using standard techniques to measure activity level, anxiety-like behavior, social behavior, and acoustic startle / prepulse inhibition. Results: SERT 56Ala variant mice exhibit elevated whole blood 5-HT. Initial behavioral studies suggest social and sensory alterations in the SERT 56Ala variant mice. Conclusions: The SERT 56Ala mouse is the first mouse model targeting an autism-associated gene to manifest hyperserotonemia. Initial studies provide preliminary support for altered behavioral traits with face validity for autism spectrum disorder. Ongoing efforts seek to connect the intermediate steps between the SERT 56Ala variant and the observed neurochemical and behavioral phenotype.

Oral Presentations Program
123 School/Memory/Mentalizing

123.00 Mediators of Student Success in a Randomized Controlled Study of Teacher Consultation in Autism: a Preliminary Investigation Establishing Proof of Concept. L. A. Ruble*[1] and J. H. McGrew[2], (1)*University of Kentucky*, (2)*Indiana University - Purdue University Indianapolis*

Background:

The increasing numbers of students with autism combined with the limited number of teachers with training in autism presents a serious issue in providing effective services and producing positive educational outcomes. Child-specific teacher consultation is often employed as an indirect method of influencing teacher behavior with the hope that it will positively impact educational quality and child outcomes. Although consultation research is promising, very little has been targeted in autism. Moreover, the existing research is based on pre-post designs and has paid little attention to examining potential mediators of change. Preliminary evidence suggests that one model of teacher consultation, the Collaborative Model for Promoting Competence and Success (COMPASS; Ruble & Dalrymple, 2002) can impact outcomes for children with autism; however, information is lacking on the active ingredients of the consultation.

Objectives:

To identify possible mediators of COMPASS consultation that may be useful in understanding the therapeutic mechanisms of action, and help in establishing proof of concept of how COMPASS causes change in teacher behavior and child outcomes.

Methods:

A randomized controlled design was used to determine the effectiveness of COMPASS consultation and teacher coaching sessions on teacher, parent, and child outcomes. Thirty-five teachers were randomly assigned to (a) COMPASS and teacher coaching or (b) services as usual group (SAU; regular school program based on the child's IEP). All participants completed a pre- and post-evaluation. Following the pre-evaluation, teachers were randomly assigned to either the experimental or the SAU condition. Eighteen teachers in the experimental condition participated in a half-day consultation that included the parent. Three skills were prioritized and specific teaching plans were generated. Following consultation, teachers also received four 1.5 hour teacher-coaching sessions. Two potential mediating variables, IEP quality and teacher adherence to the intervention, were examined to establish proof of concept.

Results:

Children in the treatment group (N=18) made significant progress on targeted IEP objectives based upon evaluation by an observer unaware of group assignment compared to control group children. Prior to the consultation, IEP quality was similar for the experimental and control conditions. After COMPASS consultation, however, IEP quality was higher in the experimental condition. Teacher adherence to the teaching plan was significantly higher at time 2 compared to time 1 and was significantly associated with child outcomes at time 4.

Conclusions:

Preliminary data suggest that IEP quality is important for ensuring child success in meeting educational goals. Also, teacher coaching and

follow-up also appear to be essential elements to ensure treatment implementation. These findings suggest critical areas for future research to improve teacher training efforts in autism.

123.01 The Effects of a Randomized Controlled Social Skills Intervention on Peer Relationships and Social Networks of Children with Autism in the School Setting. C. Kasari*[1], J. Locke[1], A. Gulsrud[1] and E. Rotheram-Fuller[2], (1)*University of California, Los Angeles*, (2)*Temple University*

Background: Several peer intervention models have been employed to remediate social skills in children with autism; however, these models have not been subjected to systematic comparison, nor have they been implemented in regular school programs for school-aged children.

Objectives: This study examined the effects of intervention (child- or peer-mediated, combined, or no intervention) on the peer relationships and social networks of children with autism.

Methods: Participants included 60 fully-included children with autism (54 male, 6 female) and 1786 typically-developing children. All were recruited from grades 1-5 from 56 classrooms in 30 different schools across the Los Angeles area. They were an average of 8.14 years old (SD=1.56), with an average IQ of 90.97 (SD=16.33). Children with autism and their peers completed a friendship survey at the beginning and end of a 12 session, 6-week social skills intervention that was coded following the methods outlined in Cairns and Cairns (1994). All intervention sessions occurred at the target child's school during recess periods twice a week. Each child with autism was randomly assigned to the peer-mediated, child-mediated, combined, or no intervention (control) and received a follow-up visit 3 months after the intervention.

Results: Social network ratings, number of received friendship nominations, and the percentage of reciprocal three best friendships were analyzed using a multilevel random coefficient model in SAS Proc Mixed 9.1. Results indicated a significant treatment group by time interaction, $F(8, 56) = 2.16$, $p<.05$. Children with autism who received the combination treatment had higher social network ratings compared to children in the control condition $t(8, 56)=2.71$, $p<.01$. Children with autism in the child-mediated condition did not significantly differ in social network ratings after treatment from children in the control condition. A treatment group by time interaction was also significant for children's number of received friendship nominations, $F(8, 56) = 2.42$, $p<.05$. Children with autism in the peer-mediated treatment had more friendship nominations after treatment as compared to children in the control condition, $t(8, 56)=2.10$, $p<.05$. Lastly, results indicated that the percentage of children's three reciprocal best friendships was significantly different across groups, $F(3, 53) = 3.39$, $p<.05$, such that children with autism in the child-mediated condition had significantly fewer reciprocal three best friendships in comparison to children in the peer-mediated $t(3, 53)=-2.37$, $p<.05$, combined $t(3, 53)=-2.28$, $p<.05$, and control $t(3, 53)=-2.94$, $p<.01$ conditions.

Conclusions: This study reports changes in children's social network ratings and friendships in 12 school-based intervention sessions. Social skills can be taught to children with autism and the best avenue to do so is through a multi-agent model that involves the target child and typically-developing peers. Targeting only the child with autism did not improve the child's social position in the class or reciprocated friendships suggesting that an adult-mediated one-on-one approach at school may be more stigmatizing to the child, setting him/her apart from his/her classmates. Treatment effects faded somewhat over time for all children suggesting that children likely need continued support in the school setting.

123.02 Helping High-Functioning Students with Autism Spectrum Disorder Overcome Their Reading Problems: a Randomized Field Study. C. Roux* and E. Dion, *University of Quebec in Montreal*

Background: Students with Autism Spectrum Disorder (ASD) have a tendency to learn by rote without necessarily making sense of what they learn (Rutter, 1985), something that can notably be observed in their patterns of reading ability. Indeed, ASD students often show evidence of atypical profiles of reading ability. These students seem to present age appropriate or higher word recognition abilities and little or no comprehension (e.g., Whitehouse & Harris, 1984). Although there is now evidence that some students with ASD seem to demonstrate close to or age appropriate reading comprehension abilities, more than half of theses students show important reading difficulties. Further, there seems to be a positive relationship between these students comprehension ability and their oral vocabulary

(Nation et al., 2006). Objectives: The purpose of this study was to evaluate the effectiveness of a highly structured small group reading comprehension instruction, which combines vocabulary and main idea identification instruction specifically designed for ASD students. Methods: 43 ASD students (7-11 years old) with end of first-grade or better word recognition ability participated in the study. Small groups (3 or 4 students) were paired on pre-test measures then randomly assigned to either an intervention condition or to a control condition. The control group received regular instruction only. The students participating in the intervention condition received 24 hours of reading comprehension instruction. They received instruction three times a week (30 minutes per session) for a period of 16 weeks. The intervention combined decoding of multi-syllabic words, word meaning (vocabulary), reading of connected text, main idea identification (Carnine et al., 2004) and story structure (Williams et al., 2001) instruction. Results: The results show statistically significant effects on researcher-developed measures of instructed vocabulary $F(1, 42) = 6.59$, $p < .05$, $d = 0.8$, main idea identification skills $F(1, 42) = 7.423$, $p < .05$, $d = 0.7$, and general comprehension skills $F(1, 42) = 4.013$, $p < .05$, $d = 0.6$. Conclusions: The present results suggest that intensive and highly structured interventions are efficient to teach word meaning and main idea identification skills to ASD students, as well as general text comprehension. These results have important implications for the development of future effective reading comprehension interventions.

123.03 Discriminant Analysis and Reliability Evaluation of Fidelity Measures for Comprehensive Treatment Models Serving Young Children with Autism Spectrum Disorders.

K. Hume*[1], B. Boyd[2], D. Coman[3], A. Gutierrez[3], E. Shaw[1], L. Sperry[4], M. Alessandri[3] and S. Odom[5], (1)*Frank Porter Graham Child Development Institute, University of North Carolina, Chapel Hill*, (2)*FPG Child Development Institute*, (3)*University of Miami*, (4)*University of Colorado Denver*, (5)*University of North Carolina*

Background:

Few comprehensive treatment models serving preschool aged children with ASD have well-developed measures of fidelity of implementation, and for the measures that do exist we know very little about their psychometric properties (i.e. reliability and validity). This is of great concern as fidelity tools must adequately measure the quality / degree of implementation to ensure successful adoption and replication of a model. Effective implementation of a comprehensive model, as measured by empirically validated fidelity tools, should have a direct impact on child outcomes.

Objectives:

This study empirically-validated treatment fidelity measures for two existing comprehensive treatment models-- Division TEACCH and LEAP, and a measure for non-model specific, eclectic classrooms serving children with ASD. The goals were to determine if these three instruments were reliable and could discriminate between preschool classrooms using TEACCH, LEAP, or an eclectic treatment approach (termed "Business as Usual or BAU" for study purposes).

Methods:

Research staff across three states was trained in the use of each fidelity measure and met criterion for inter-rater reliability. Generally, 4 observations were then conducted in 11 TEACCH, 10 LEAP, and 13 BAU preschool classrooms serving students with ASD across study sites over a four month period. During each classroom observation all 3 fidelity measures were completed. The reliability of the measures was determined by examining test-retest reliability, internal consistency, and interrater agreement. Discriminant analysis was conducted to examine the subscales of each measure that most contributed to the ability of the fidelity measure to discriminate model types.

Results:

Test-retest reliability for the four observations was M = .77 for the BAU measure (.53-.86 across 8 subscales), M = .61 for the LEAP measure (.45-.86 across 8 subscales), and M = .63 for the TEACCH measure (.43-.86 across 9 subscales).

Internal consistency was examined using Cronbach's alpha. For the BAU measure, the alpha was.94 (.71-.95), .93 for LEAP (.55-.90), and .93 for TEACCH (.42-.93).

Inter-rater reliability was measured as the proportion of agreement between observers. Inter-rater reliability was 93% (BAU, 82-97%), 95% (LEAP, 82-100%), and 89% (TEACCH, 87-96%), respectively.

Discriminant analyses were performed to identify the subscales of the fidelity measures that best discriminated between classroom types. On the BAU measure, two subscales-- *social/peer relations* and *curriculum and instruction* primarily contributed to the ability of the measure to discriminate between the 3 treatment models. On the LEAP measure *social interaction* and *teaching communication subscales* best contributed to the discrimination between model types, and on the TEACCH measure four subscales, *communication, assessment, visual schedules,* and *social* discriminated between the models.

Conclusions:

Results indicate that the TEACCH, LEAP, and BAU fidelity measures are psychometrically robust and clearly discriminate between the intervention models. Both the development/adaptation of these measures and the analyses of their psychometric properties are significant contributions to the field. The strength and impact of the intervention relies on accurate and measurable implementation.

123.04 Remembering the Past and Imagining the Future Amongst Individuals with Autism. S. E. Lind* and D. M. Bowler, *City University, London*

Background: Recent research has indicated that the same neurocognitive system that underlies the capacity to remember past experiences (episodic memory) also underlies the capacity to imagine future experiences (prospection) (Buckner & Carroll, 2007; Hassabis & Maguire, 2007; Spreng et al., in press). Indeed, this discovery was considered to be one of the major scientific breakthroughs of 2007 (The News Staff, 2007, *Science*, *318,* 1844-1849). It is established that individuals with autism have diminished episodic memory (see Boucher & Bowler, 2008). However, very little research has sought to assess prospection amongst individuals with autism. Prospection is essential for flexibility of thought and action because it enables one to simulate and predict future scenarios, thereby allowing one to plan and select the optimal course of action. Thus, impairments in this domain may help to explain why individuals with autism exhibit restricted, repetitive and stereotyped patterns of behaviour. Difficulty in acting with the future in mind may result in over-dependence on routinised, inflexible patterns of behaviour.

Objectives: The main aims of this study were to establish: (a) whether prospection as well as episodic memory is impaired amongst individuals with autism; (b) whether prospection and episodic memory are related amongst people with autism; (c) whether imagined and/or remembered events differ qualitatively between individuals with and without autism; (d) the extent to which predicted impairments in prospection contribute to behavioural inflexibility amongst individuals with autism.

Methods: Participants were high-functioning adults with autism and typical adults who were matched on age, sex, verbal IQ and performance IQ. Autism diagnoses were confirmed using the Autism Diagnostic Observation Schedule (Lord et al., 1999) and all participants completed the Autism Quotient (Baron-Cohen et al., 2001). The experimental task was based on one used previously by D'Argembeau and Van der Linden (2004) with typically developing adults. Participants were prompted to recall seven specific events from the past and to imagine seven specific likely-to-occur events in the future. In order to assess the subjective qualities of these memories/images, participants were asked to complete an adapted version of the Memory Characteristics Questionnaire (MCQ) (Johnson et al, 1988) for each event. Participants were also tested for word, category, and ideational fluency.

Results: Preliminary results, based on 22 participants (more data are currently being collected), indicate that: (a) individuals with autism showed higher response latencies, and were less likely to recall/imagine specific past/future events (even after controlling for fluency); (b) within each group, the capacity to recall the past was correlated with the capacity to imagine the future; (c) remembered/imagined events differed qualitatively between participants with and without autism on a number of dimensions (as determined by subjective ratings on the MCQ); and (d) among individuals with autism, impairments in prospection were related to impairments in behavioural flexibility.

Conclusions: These results have implications for our understanding of the inflexible behaviour that characterises autism, suggesting that difficulties with imagining future events may impact upon the capacity of individuals with autism to plan and act for the future.

123.05 Eye Tracking Reveals Impairments in Implicit Mentalizing in Adults with Asperger's Disorder. A. Senju*[1], V. Southgate[1], S. White[2], D. Coniston[2] and U. Frith[2], (1)*Birkbeck, University of London*, (2)*University College London*

Background: Paradigms now exist that demonstrate that preverbal children anticipate others' actions based on their false beliefs well before they can understand standard False Belief tasks. One such paradigm using eye tracking has recently shown that children with ASD, aged 6 to 8 years, who *fail* explicit false belief tasks, also lack the implicit mentalizing ability demonstrated in preverbal children. What about adults with Asperger's Disorder who *pass* explicit false belief tasks? Would they nevertheless lack the implicit and spontaneous ability to mentalize? Eye tracking methodology can answer this question. However, the relevant paradigms have never been tried with adults.

Objectives: To test the hypothesis that adults with Asperger's Disorder, while passing explicit false belief tasks, will still show an implicit and spontaneous deficit in mentalizing. Specifically, whether they would fail to anticipate actions based on others' false beliefs, as revealed by their eye gaze.

Methods: We presented video stimuli of an actor watching an object being hidden in a box. The object was then displaced while the agent was not attending. We recorded participants' eye movement with an eye-tracker while they watched the agent's subsequent action and coded whether participants spontaneously anticipated the actor's behaviour (*i.e.* reaching for the location where the agent had last seen the object), which could only have been predicted based on her false belief. 19 adults with Asperger's Disorder, (IQ above 85) as well as 17 neurotypical adults, participated in this study. The study was approved by the UCL Research Ethics Committee. Participants gave informed written consent.

Results: Neurotypical adults anticipated (by looking at the window through which she would reach) the agent's action based on her false belief ($p < .05$, binominal test). Asperger adults did not show such anticipatory looking ($p > .1$, binominal test). In addition, neurotypical adults spent significantly longer looking at the correct location than Asperger adults (F (1,32) = 4.93, $p < .05$, $\eta_p^2 = .134$).

Conclusions: Eye tracking revealed that adults with Asperger's Disorder, despite being able to take into account others' mental states when explicitly required to do so in standard verbal tasks, lacked the spontaneous and implicit ability to anticipate other's actions in non-verbal False Belief tasks.

Oral Presentations Program
124 Face Processing

124.00 Facial Recognition, Configural Processing, and Concept Formation in High-Functioning Autism. N. J. Minshew*[1], K. E. Bodner[1] and D. L. Williams[2], (1)*University of Pittsburgh School of Medicine*, (2)*Duquesne University*

Background: Individuals with autism have been reported to have impairments relative to age and ability-matched controls on tests of facial recognition. It has been proposed that difficulty with face recognition may be related to a more general problem with configural processing or, alternatively, a problem with prototype formation and expertise development.

Objectives: The purpose of the study was to investigate the relationship between face recognition abilities and measures of configural processing and concept formation in individuals with high-functioning autism (HFA) as compared to age and ability-matched controls with typical development (TD).

Methods: Participants were 36 HFA (10–38 years; mean = 18.9 years) and 30 age and IQ-matched TD controls (10-42 years; mean = 20.9 years). All participants received the Benton Facial Recognition test (BFRT), the Block Design subtest (BD) of the Wechsler Abbreviated Scale of Intelligence (WASI), the Embedded Figures Task (EFT), and the Vygotsky Concept Formation test (VCF). Autism diagnosis was established by the ADOS and ADI, and confirmed by expert clinical impression. All participants attained Full Scale IQ scores>80 (HFA mean= VIQ 104.3; PIQ 105.8; FSIQ 105.6; TD mean= VIQ 107.4; PIQ 107.0; FSIQ 108.4).

Results: There was a significant difference in performance between groups on the BFRT [$F(1,64)=17.14$, $p=.000$], with individuals with HFA performing more poorly than TD individuals. HFA participants had significantly lower total correct scores than the TD participants on the EFT, [$F(1,64)=7.3$, $p=.008$]. There were no significant group differences on BD or a measure of concept formation from the VCF test. There was

a significant positive correlation between BFRT raw scores and EFT total correct scores for the HFA participants ($r = .43$, $p < .01$); no significant correlation between these measures was obtained for the TD participants. There were no other significant correlations. Further exploration of the relationship between these measures using a multiple regression model indicated that diagnosis [$t(63) = -3.21$, $p = .002$] and performance on EFT [$t(63) = 2.91$, $p = .005$] are significant predictors of performance on the BFRT ($R^2=.31$).
Conclusions: These individuals with autism and without intellectual disability exhibited poor performance on both the Benton Facial Recognition Test and the Embedded Figures Test with positive correlations between these scores. The positive correlation between these scores suggests that these individuals with autism are using local processing abilities or feature-based processes to identify faces. The lack of correlation between face processing measures and more general processing measures may mean that these are unrelated domains or entirely separate and unrelated processes in the brain or these measures have limitations that obscure relationships.

124.01 Attentional Abnormalities in Young Children with ASD: Limited Capture by Socially Relevant Stimuli. K. Chawarska*, F. R. Volkmar and A. Klin, *Yale University School of Medicine*

Background:

Young children with Autism Spectrum Disorders (ASD) exhibit atypical scanning patterns and poor face recognition. It is not clear, however, if face processing deficits are also expressed at a basic attentional level, as manifested through decreased attention capture by faces. When typically developing children and adults are engaged in examining a face, shifting visual attention away from the face is more effortful than shifting away from other classes of stimuli. This increased attention capture by faces is thought to reflect deeper level obligatory processing triggered by these highly socially and biologically relevant stimuli.

Objectives:

To examine if attention capture by faces is disrupted in the early developmental stages of ASD.

Methods:

Children with ASD (M_{age}=32 months, N=42) were compared with developmentally delayed (M_{age}=29 months, N=31) and typically developing (M_{age}=29 months, N=46) children. Attention capture was tested using a variation of the overlap cued attention task in which participants were required to disengage visual attention from face or non-face central stimuli and make a reactive saccade to a peripheral target. Main outcome measure consisted of saccadic reaction time (SRT). The experimental protocol was approved by the Human Investigations Committee and an informed written consent was obtained from all parents prior to the testing.

Results:

Disengaging from a face as measured by SRT was more difficult for developmentally delayed ($p < .001$) and typically developing children ($p < .021$) than for those with ASD, suggesting that their attention is not captured by faces to the same extent as in their comparison groups. This effect appeared specific to faces and was not observed in response to non-face stimuli, where SRT was comparable in all three groups.

Conclusions:

The results suggest that face processing difficulties in children with ASD involve disruption of an elementary attentional mechanism that typically supports obligatory processing of face stimuli. Findings are discussed in the context of a developmental model of face processing in ASD.

124.02 Is Face Recognition Really Impaired in Autism Spectrum Disorders? the Role of Gaze Direction. S. R. Zaki*[1] and S. A. Johnson[2], (1)*Williams College*, (2)*Dalhousie University*

Background: Face recognition is often, although not always, reported to be impaired in high functioning individuals with an autism spectrum disorder (ASD). One potential explanation for this deficit is motivated by findings that face recognition might be a type of expertise. That is, individuals with an ASD may not develop expertise in face perception because of less time spent looking at faces (e.g., Gretolli, Gauthier, & Schultz, 2002). There is some evidence that participants with autism tend to avoid looking at others, and especially looking at the region of the eyes (e.g., Kanner, 1943; Langdell, 1978; Osterling & Dawson, 1994). Thus, it is possible that lack of social interest underlies face

recognition deficits in autism. A related, but slightly different hypothesis, is that the aversion to eye contact in ASD that is often reported clinically may play a role in reported face recognition deficits. A test of this hypothesis stems from social cognition studies that have shown that typically developing children and adults better remembered faces in which the eyes were directly gazing at them compared to faces in which the eyes were averted (e.g., Hood, Macrae, Cole-Davies & Melanie Dias, 2003).
Objectives: We tested the hypothesis that, in contrast to findings in typically developing individuals, face recognition in ASD would not be facilitated by direct gaze. Instead, we expected to find the opposite pattern in the ASD participants: better performance for averted gaze faces relative to direct gaze faces.
Methods: Eighteen high functioning children and adolescents with an ASD and 19 age and IQ matched typically developing controls were shown a series of images of faces. The gaze of the face was either direct or averted. We then tested memory for these faces in an old/new recognition task. All faces in the old/new recognition task were shown with their eyes closed.
Results: A group by condition (direct gaze, averted gaze) ANOVA revealed a group by condition interaction, $F(1,35)=5.2$, $p<.05$, but no main effect of group or condition. The general pattern of results suggested that the typically developing group better remembered the direct gaze faces than the averted gaze ones, whereas, in contrast, the ASD participants showed the reverse effect. Interestingly, there was no difference between groups for recognition of faces with averted gaze (controls = 59%, ASD = 63%), whereas the ASD group recognized fewer direct gaze faces (54%) than the control group (67%; $t=-2.21$, $p < .05$).
Conclusions: These results imply that the direction of gaze plays a critical role in face recognition performance in those with an ASD. There may be an important link between gaze aversion in ASD and face recognition abilities. Given that previous studies have primarily used face stimuli with direct gaze, it is important to consider conclusions about "impaired" face processing in light of the current study.

124.03 Perceptual Matching of Facial Expressions and Identities in Children with Autism Spectrum Disorders. K. Evers*[1], J. Steyaert[2] and J. Wagemans[3], (1)*Katholieke Universiteit Leuven*, (2)*UPC-K.U.Leuven*, (3)*Katholieke Universiteit Leuven, Belgium*

Background: Children with autism have a perception which fundamentally differs from ours. According to the Weak Central Coherence theory, children with autism experience difficulties with central coherence and, as a consequence, they have difficulties in holistic processing (e.g., of faces) and they have a processing bias for details. According to the Enhanced Perceptual Functioning hypothesis, children with autism have superior qualities in detecting and discriminating stimuli. Moreover, children with autism have difficulties with dynamic stimuli and in filtering out irrelevant details.

Objectives: Using dynamic face stimuli, we wanted to investigate possible strengths and weaknesses in the perception of children with autism. In particular, we examined whether they were better or worse in matching tasks that required focusing on the identity or the emotion of faces with dynamic facial expressions.

Methods: Two groups of 24 boys, matched for age (M = 9 y, range between 7 and 11 y) and IQ (M = 104, range between 90 and 120), were tested. One group had received the clinical diagnosis of autism based on DSM-IV criteria and ADI-R scores, without attention or concentration problems and using no medication. The control group was representative for the general population, in the same range of intelligence. The stimuli consisted of faces of four different female adults expressing four different emotions: happiness, anger, surprise, disgust. Each trial consisted of a series of 25 consecutive images showing the expression dynamically (25 fps), followed by a blank interval (1 s) and a static test frame. Participants had to indicate whether the static test frame was same or different as the series preceding it. In one block of trials, the matching criterion was identity, in another block it was emotion. In both identity and emotion matching, the irrelevant aspect (emotion and identity, resp.) could be congruent or incongruent.

Results: The autism group tended to perform worse and slower than the control group but the overall group differences were small. Identity matching was easier than emotion matching. More interestingly, there was a large interaction effect of task and group: The autism group performed

worse and slower than the control group on emotion matching, while they performed equally well and fast on identity matching. Congruent trials were performed better and faster than incongruent trials in both groups. Both groups were faster at congruent than incongruent match trials. Moreover, the autism group, but not the control group, appeared faster on the incongruent different trials than on the congruent different trials. In other words, an irrelevant difference was beneficial for the autism group only.

Conclusions: We did not find large difficulties in processing the dynamic face stimuli. Task difficulty and group differences depended on the specific task requirements. Children with autism performed equally well as control children on identity matching but they were less good and slower at matching facial expressions regardless of identity. Children with autism were faster when the task-relevant differences between stimuli were accompanied by task-irrelevant differences, whereas control children filtered these out more efficiently.

124.04 An Investigation of Social-Perception Strategies in the Broad Autism Phenotype: Integrating Eye Tracking and Behavioral Methodologies. K. P. Wilson*, M. Losh and P. C. Gordon, *University of North Carolina at Chapel Hill*

Background: The Broad Autism Phenotype (BAP) is a cluster of social, language, and personality features representing subtle expressions of autism characteristics, found in non-autistic relatives of individuals with autism (Pickles et al., 2000). Social features of the BAP are related to deficits in social-cognition (Losh & Piven, 2007), though the neurocognitive mechanisms underlying these traits are not fully understood. Investigation of perceptual strategies during social-cognitive tasks may further clarify underlying neurocognitive mechanisms. Existing eye tracking studies of individuals with autism describe atypical fixation patterns when processing social stimuli. In contrast to controls, who focus mainly on the eyes, individuals with autism fixate on less salient regions, such as mouths, bodies, and objects (Klin et al., 2000). Similar patterns have been noted in the BAP (Adolphs et al., 2008); however, investigation of fixation patterns during a variety of social-cognitive tasks is needed to clarify these patterns and detect links to underlying neurocognitive mechanisms.
Objectives: This study employs eye tracking to investigate the relationship between face scanning strategies and behavioral responses during a social-cognitive task with established ties to discrete brain regions, and the amygdala in particular. For this study, a sample of BAP+ parents was selected from a previous study based on severely aberrant social-cognitive performance, with the goal of investigating further the underlying features of their unique profile.
Methods: Five BAP+ parents of children with autism were tested [with additional data collection underway (target BAP+ n=15, Control n= 15)]. Clinical characteristics of the BAP were assessed using established, valid and reliable tools for discriminating parents of individuals with autism from controls. Behavioral data were collected using the social-cognitive task, 'Trustworthiness of Faces', which requires evaluation of 42 faces varying in hedonic tone for trustworthiness cues. Tobii 1750 equipment captured eye tracking data during this task to discern processing strategies through comparison of fixation patterns to behavioral responses.
Results: In contrast to typical scan patterns described in the literature, showing primary fixation on the eyes (Walker-Smith et al., 1977), BAP+ participants focused preferentially on the nose, with only slightly greater fixation on the right eye. In positively-normed (i.e., "friendly") slides, subjects looked substantially more at noses than mouths, despite the informative nature of smiles in these slides. Analyses of fixation patterns in relation to ratings of trustworthiness revealed that BAP+ participants assigned negative ratings to both positive (i.e. trustworthy) and negative (i.e. not trustworthy) faces, compared to norms.
Conclusions: Preliminary eye tracking data implicate perceptual processing strategies that may elucidate the basis of the mild social-cognitive impairments previously documented among autism parents who demonstrate the social features of the BAP. In particular, the tendency of the BAP group to rate all faces, both positive and negative, as untrustworthy, coupled with the atypical fixation on non-salient facial features (i.e., noses), suggests that aberrant facial scanning strategies affect interpretation and judgment of social information.

124.05 Seeing Things That Aren't There: Perception of Faces and Objects in Visual White Noise in Autism and Asperger's Syndrome. H. S. Cheang*[1], L. Mottron[2] and B. Jemel[3], (1)*Rivière-des-Prairies Hospital/University of Montreal*, (2)*Centre d'excellence en Troubles envahissants du*

développement de l'Université de Montréal (CETEDUM), (3)*Hopital Riviere des Prairies/University of Montreal*

Background: Typical adults exposed to unstructured white noise report having perceived a smile on a face when they had been told that there might be a smiling face in the noisy image (Gosselin & Schyns, 2003). This induced illusory ("superstitious") perception does not originate from the input signal (i.e. white noise), but from top-down influences on visual analyses of uninformative signals. Such tasks can help answer questions regarding the known but relatively unquantified atypical top-down processing mechanisms of persons with autistic spectrum diagnoses.

Objectives: Our goal was to investigate whether superstitious perception differed across groups of autistic and Asperger syndrome (AS) individuals and their age-and IQ-matched typical controls, as a means of discerning differences in top-down processing of visual stimuli in these populations.

Methods: Three groups of participants, autistic (N=13, Age=26 yrs, FS-IQ=104), AS (N=10, Age=24 yrs, FS-IQ=105), and typical (N=12, Age=24 yrs, FS-IQ=108) adults, were presented with face (half male, half female) and object (half animate, half inanimate) images embedded in a fixed level of visual white noise, as well as with images of pure visual white noise. At the beginning of half of the trials, the textual cues of "FACE" and "OBJECT" were visually displayed prior to the presentation of a category-consistent stimulus or a visual noise stimulus. Participants were instructed to make a male/female judgment whenever a face appeared and an animate/inanimate judgment whenever an object appeared. Conversely, if they were uncertain of what they had perceived, they were to give an answer of "I don't know". Participants indicated their responses by pressing one of three buttons. Proportions of responses to individual categories of presented stimuli were analysed via separate mixed design analyses.

Results: When presented with objects in noise, AS participants showed a significant tendency to give "I don't know" responses more often than the other two groups for both cued ($p=0.006$) or non-cued stimuli ($p=0.03$). When presented with white noise images, typical adults were significantly more likely than both autistic and AS participants to report face or object perception (by giving a response of "male", "female", "animal" or "object"). Autistic and AS groups were further distinguished from one another. Whereas autistic subjects gave comparable proportions of both face/object responses and "I don't know" responses, nearly *all* of the responses to noise stimuli by AS participants were "I don't know" ($p<0.001$ all cases).

Conclusions: Behaviourally, a gradient of susceptibility to superstitious perception can be inferred: typical adults are highly susceptible; autistic adults somewhat susceptible; and AS adults appear unsusceptible. Perhaps more importantly, the present data suggest that while top-down processing drives typical visual perception, bottom-up processes mediate the perception of persons with autistic spectrum diagnoses. In the specific case of AS adults, perception may be driven exclusively by bottom-up processes.

Funding provided by an Autism Speaks Postdoctoral Fellowship Award to the first author and a NAAR operating grant to the third author.

Oral Presentations Program
125 Molecular Genetics II

125.00 Dendritic Trafficking & ASDs: Convergent Evidence Identifying MAP/Microtubule Affitiny-Regulating Kinase ( ) as a Susceptibility Gene for Autism. M. J. Simonneau*[1], G. Maussion[1], J. Carayol[2], A. M. Lepagnol-Bestel[1], F. Tores[2], Y. Loe-Mie[1], U. Milbreta[1], F. Rousseau[2], J. Renaud[3], J. M. Moalic[2], A. Chedotal[4], P. Gorwood[1], N. Ramoz[1] and J. Hager[2], (1)*INSERM*, (2)*IntegraGen SA*, (3)*INSERM U592*, (4)*INSERM U968, Institut de la Vision*

Background:

Autism spectrum disorders (ASDs) are genetically heterogeneous neurodevelopmental conditions. Application of a direct physical identity-by-descent mapping approach to perform a high-density genome-wide linkage allowed the identification of novel loci (Philippi et al, 2005, Molecular Psychiatry).

Objectives: The objective of this work was to identify an associated gene on chromosome 1q41-q42 and to define its functional involvement in ASDs.

Methods: Association studies in 276 ASD families from the Autism Genetic Research Exchange, measurements of *MARK1* transgene expression as

a function of human regulatory region haplotypes, quantification of transcripts in post-mortem human brain tissues from Autism Tissue Program and in vitro analysis of *Mark1* overexpression and down regulation by shRNAs in mouse cortical neurons have been performed.

Results:

High-resolution genotyping of 126 single-nucleotide polymorphisms across the 1q41-q42 region, followed by a *MARK1*-tagged-SNP association study allowed to identify *MARK1* SNPs significantly associated with ASDs by transmission disequilibrium tests. Furthermore, haplotype rs12740310*C-rs3737296*G-rs12410279*A was overtransmitted (Pcorrected=0.0016) with a relative risk for autism of 1.8. The transcription level of *MARK1* is modulated by the ASD-associated SNP rs12410279. *MARK1* is overexpressed in the prefrontal cortex (BA46) but not in cerebellar granule cells from patients. Accelerated evolution displayed by MARK1 along the lineage leading to humans suggests a possible involvement of this gene in cognition. MARK1 encodes a kinase-regulating microtubule-dependent transport in axons and dendrites. Both overexpression and silencing of MARK1 showed a significantly shorter dendrite length in mouse neocortical neurons and modified dendritic transport speed. MARK1 is involved in axon-dendrite specification, as expected for a gene encoding a key polarity determinant Par-1 protein kinase.

Conclusions: MARK1 could be responsible for subtle changes in dendritic functioning in ASD patients. We previously reported that SLC25A12 is associated with neurite outgrowth and is upregulated in the prefrontal cortex of autistic subjects (Lepagnol-Bestel et al, 2008, Molecular Psychiatry). Altogether these results demonstrate that deregulations of genes encoding proteins involved in dendritic trafficking can contribute to ASDs.

Human brain samples were obtained from Autism Tissue Program. This work was partially funded by INSERM, Fondation Orange and ANR.

125.01 Novel Variants Identified in Methyl-CpG-Binding Protein Genes in Autistic Individuals. H. N. Cukier*[1], R. Rabionet[2], I. Konidari[1], M. Y. Rayner[2], M. L. Baltos[2], H. H. Wright[3], R. K. Abramson[3], M. L. Cuccaro[1], M. A. Pericak-Vance[1] and J. R. Gilbert[1], (1)*University of Miami Miller School of Medicine*, (2)*Miami Institute for Human Genomics*, (3)*University of South Carolina School of Medicine*

Background: Misregulation of the *methyl-CpG-binding protein 2* (*MECP2*) gene causes a myriad of neurodevelopmental disorders characterized by social and intellectual impairments - most notably Rett syndrome and some cases of autism. We hypothesized that mutations in additional members of the methyl-CpG-binding family (*MBD1, MBD2, MBD3* and *MBD4*) may also be involved in autistic spectrum disorders (ASD). This is further supported by evidence that different MBD proteins are capable of binding the same promoter region, suggesting a functional interdependence. To date, only one study has evaluated the MBD genes of autistic patients and was limited to a Japanese population. A single variation of interest was identified, R269C in MBD1.

Objectives: To evaluate the *MBD1*, *MBD2*, *MBD3* and *MBD4* genes for possible alterations that may be associated with autism.

Methods: In this study, 226 autistic individuals (195 Caucasians (CA) and 31 African-Americans (AA)) were evaluated for the coding regions of *MBD1-4* by denaturing high performance liquid chromatography and results were confirmed either by TaqMan or direct sequencing. We used both multiplex and singleton families and examined transmission and disease concordance. When available, additional family members were tested for segregation of variations identified in the proband.

Results: We identified 198 autistic individuals (167 CA and 31 AA) carrying genetic alterations at 46 unique loci. 20/46 of the variations were known single nucleotide polymorphisms (SNPs), while 26/46 were novel (5 insertion/deletions and 21 SNPs). While the majority of alterations were synonymous or noncoding SNPs, we identified 12 changes to amino acid sequence. These encompassed 10 missense changes in MBD1, 3 and 4, a deletion of a single amino acid in MBD3, and a frameshift mutation in MBD4 that is predicted to truncate almost half of the protein. Five of the nonsynonymous changes were found exclusively in singleton families. The novel MBD3 R23M and E281del alterations were each found to segregate within the multiplex families where they were identified. The MBD4 S342P variant was

found to segregate in 4 of the 5 multiplex families in which it occurred and the remaining nonsynonymous changes did not consistently segregate. We did not identify the MBD1 R296C variant. Sixteen of the novel single nucleotide changes and four of the deletions were not found in 300 CA or 188 AA control alleles. Furthermore, unaffected family members that also carry MBD variations present a range of psychiatric and developmental disorders including anxiety/panic disorder, depression, speech delay and learning disabilities.

Conclusions: We identified variations that could lead to alterations in RNA or protein structure and may result in functional changes. Results from these rare variants indicate a potential role for the MBD genes in the molecular and genetic etiology of autism.

125.02 BDNF/TRKB Signalling Pathway in Autism: Increased Plasma BDNF Levels and Association of NTRK2 Genetic Variants in An Autism Population Sample. C. Correia[1], A. Coutinho[2], S. Silva[2], I. Sousa[2], L. Lourenço[2], J. Almeida[3], R. Lontro[3], C. Lobo[3], T. S. Miguel[3], L. Gallagher[4], M. Gill[4], S. Ennis[5], T. Magalhães[1], G. Oliveira[3] and A. Vicente*[1], (1)*Instituto Gulbenkian de Ciência/Instituto Nacional de Saúde Dr. Ricardo Jorge*, (2)*Instituto Gulbenkian de Ciência*, (3)*Hospital Pediátrico de Coimbra*, (4)*Trinity College Dublin*, (5)*National Center for Medical Genetics/UCD*

Background:

Brain Derived Neurotrophic Factor (BDNF) is a member of the neurotrophin family which plays a pivotal role in the development and plasticity of the brain. BDNF has been implicated in several neuropsychiatric disorders and multiple lines of evidence suggest an involvement in autism. Direct evidence comes from reports of high serum BDNF levels in small samples of autism patients and the identification, in a large autism whole genome-linkage scan, of a *linkage* peak on chromosome 11p12-13, where the *BDNF* gene maps.

Objectives:

In this study, circulating BDNF levels were compared between autistic patients and controls, and the genetic factors that might regulate BDNF distribution and contribute to autism etiology were examined.

Methods:

BDNF levels in platelet rich plasma were measured in 146 autistic patients, 88 parents and 50 controls in the same age range. Markers selected in candidate genes, including *BDNF*, *NTRK2* (encoding the BDNF receptor TrkB), and nine genes involved in the serotonin metabolic and neurotransmission pathways (*SLC6A4*, *HTR2A*, *MAOA*, *HTR2C*, *HTR1D*, *HTR1A*, *HTR5A*, *TPH1* and *ITGB3)* were tested for association with BDNF levels. These genes were also tested for association with autism in 301 Portuguese and 168 Irish trios.

Results:

BDNF levels in autistic children were significantly higher than in control children ($P<0.0001$) and positively correlated with serotonin levels ($P=0.004$), and showed an heritability of 30%. Five polymorphisms in the *HTR1A* genomic region were associated with BDNF levels. While in the overall population association with autism was detected with four different markers in this region, in the subset of patients with high BDNF levels, four of the polymorphisms that were associated with BDNF levels were also associated with autism. These markers map not in *HTR1A* but in a neighbour gene, *RNF180*, which was very recently identified and encodes a zinc ring finger protein which functions as an E3 ubiquitin ligase. In *NTRK2* five SNPs ($0.0027<P<0.041$) and multiple two and three marker haplotypes ($0.0006<P<0.04$) were significantly associated with autism in the Portuguese population, but none were associated with BDNF levels. In the combined Portuguese and Irish sample (N=491), association was found for the same 5 SNPs, two becoming more significant, with rs1187352 and rs1187321 surviving Bonferroni correction. Although association of *NTRK2* markers could not be replicated independently in the smaller Irish sample, we found a frequent trend for overtransmission of the same alleles. No association with autism or BDNF levels of any of the other genes tested was found.

Conclusions:

We report an increase of BDNF plasma levels in 25% of the autistic children in this population sample, the largest tested thus far, corroborating previous results in smaller samples. In addition, we show that BDNF levels are heritable and that its determination is associated with genetic

polymorphisms in the chromosome 5q11.2-q13 region. We also provide evidence for an involvement of the *NTRK2* gene in autism which, taken together with the findings of increased BDNF levels, suggests that BDNF/TrkB signalling is altered in autism, possibly underlying an abnormal development of the serotonergic and glutamatergic/GABAergic systems commonly associated with autism.

125.03 The Synaptic Vesicle Gene RIMS3 Is a Novel Candidate for Autism. R. A. Kumar*[1], J. Sudi[1], T. D. Babatz[1], C. W. Brune[2], D. Oswald[3], N. J. Nowak[4], E. H. Cook[2], W. B. Dobyns[1] and S. L. Christian[1], (1)*University of Chicago*, (2)*University of Illinois at Chicago*, (3)*Virginia Commonwealth University*, (4)*University of Buffalo*

Background: Chromosomal studies and copy number variant (CNV) analysis in patients with autism spectrum disorders (ASD) have successfully led to the identification of causative and susceptibility genes. A large number of these genes are important components of the pre- and postsynaptic machineries, including *NLGN3*, *NLGN4*, *NRXN1*, *SHANK3*, and *CNTNAP2*. These observations bolster the hypothesis that autism is a 'disorder of the synapse'. **Objectives:** A child with autism and microcephaly was found to have a *de novo* 3.3-Mb deletion on chromosome 1p34. Here, we test the hypothesis that this microdeletion will contain a gene(s) that underlies the autism phenotype in this child and in other children with ASD. **Methods:** To search for submicroscopic chromosomal rearrangements in the child, we performed CNV analysis using 1) a 19K whole-genome human BAC microarray; and 2) the Illumina 610-Quad BeadChip genotyping microarray. We used Ingenuity Pathway Analysis (IPA) to construct biological networks to identify candidate genes for autism. To identify functional variants in candidate genes, we performed mutation screening using PCR-based Sanger sequencing in 512 unrelated autism patients and 465 control subjects. **Results:** We identified a 3.3-Mb deletion containing 43 genes in chromosome 1p34.2 that we confirmed using fluorescence *in situ* hybridization (FISH). Microsatellite analysis determined that the deletion was *de novo*. IPA analysis and our review of the literature identified *RIMS3* as the most promising autism candidate gene because 1) it forms biological networks with known autism genes, albeit indirectly; 2) it belongs to the RIMS protein family that constitute an important component of synaptic vesicle fusion and neurotransmitter release; 3) it is expressed in human fetal and adult brains; 4) its overexpression has been demonstrated to greatly facilitate Ca^{2+}-triggered exocytosis; and 5) mostly notably, its expression in lymphoblasts has recently been shown to be dysregulated in patients with autism. Mutation screening of *RIMS3* in 512 unrelated autism patients identified five inherited coding variants that were absent in 465 controls. One of these variants included E177A that is predicted to be deleterious and segregated with the autism phenotype in a sibship. **Conclusions:** Identification of a *de novo* microdeletion containing *RIMS3* and discovery of autism-specific *RIMS3* missense variants that segregate with autism and related phenotypes support a role for this gene in the etiology of ASD. Elucidating the functional impact of putative *RIMS3* mutations such as the E177A substitution represents an important area of investigation . Towards this end, we have obtained RIMS3- and hGH-containing vector constructs to perform Ca^{2+}-dependent exocytosis co-transfection experiments in PC12 cells to test the involvement of mutant *RIMS3* variants in synaptic function using site-directed mutagenesis.

125.04 MECP2 Is Associated with Autism. R. Delahanty*[1], E. L. Crawford[1], B. Yaspan[1], E. Kistner[2], N. Cox[2], E. H. Cook[3] and J. Sutcliffe[1], (1)*Vanderbilt University*, (2)*University of Chicago*, (3)*University of Illinois at Chicago*

Background: Autism is a neurodevelopmental disorder that affects approximately 1 in 150 individuals and is characterized by deficits in reciprocal social interaction, communication and patterns of repetitive behaviors and restricted interests. Twin and family studies indicate high heritability, but evidence supports a highly complex architecture for the underlying genetic etiology. Mutations in MECP2 give rise to Rett syndrome, which is classified as a PDD and shows many features of autism. Objectives: The objectives of this study were to test the hypothesis that common and/or rare alleles at MECP2 contribute to autism susceptibility. Methods: Using Hapmap Phase 2 data and the Tagger implementation in Haploview, we selected tag SNPs to index common alleles of the X-linked MECP2 locus. Five SNPs were genotyped in a sample of 965 combined simplex and multiplex families ascertained for idiopathic autism. FBAT and x-APL were used to test for over-transmission to affected offspring. Ancestry classification of founders was conducted using STRUCTURE and

Multidimensional Scaling (MDS) implemented in PLINK, and where necessary supplemented with self report. Exons were re-sequenced in 200 unrelated cases and 200 unrelated controls using ABI Sanger chemistry to identify rare variants. Results: For three correlated tag SNPs selected for association analysis using Caucasian HapMap data, very different allele frequencies were apparent in other HapMap populations. Initial Hardy-Weinberg calculations during QC of genotype data revealed significant deviations from HWE. Ancestry was determined using a combination of STRUCTURE and MDS analyses supplemented with self report as needed. No deviations from HWE were found within individual ethnic groups; a significant majority of the sample was of European ancestry. Significant association (e.g. 0.005 > P (x-APL) > 0.0005) was identified at these three SNPs, corresponding to an LD block containing the 3' end of the gene. This association was restricted to families of European and Hispanic ancestries, although it is likely that power to detect transmission distortion in Asian and African-American families was very limited as a function of allele frequency. Sequencing in cases and controls did not reveal evidence for a greater mutation burden in cases. However, we did identify one family in which a mother transmitted an in-frame 3bp deletion to her affected son. Conclusions: We found significant association to autism at the 3' LD block of MECP2 in families of European and Hispanic ancestry. During the course of this work, evidence for association was published (Loat et al, 2008). The SNPs reported here are in strong LD with those in Loat et al, effectively replicating that finding. We also define important population effects that impact this association. These data support a role for MECP2 in idiopathic autism attributable to common alleles. While a potentially deleterious amino acid deletion was identified, comparison of sequencing results between cases and controls reported here does not support a major role for rare variants at this time. However, further studies of rare variation at MECP2 are needed.

Oral Presentations Program
126 Infant Siblings

126.00 Comparing Prospective and Retrospective Measures of Early Language Regression in Children with Autism from a High-Risk Infant Cohort. L. Zwaigenbaum*[1], S. E. Bryson[2], J. Brian[3], I. M. Smith[2], W. Roberts[4], P. Szatmari[5], C. Roncadin[6] and T. Vaillancourt[7], (1)*University of Alberta*, (2)*Dalhousie University/IWK Health Centre*, (3)*Hospital for Sick Children & Bloorview Kids Rehab*, (4)*University of Toronto*, (5)*Offord Centre for Child Studies, McMaster University*, (6)*Peel Children's Centre*, (7)*University of Ottawa*

Background: Autism spectrum disorders (ASD) have been described as having two differing onset patterns, 'early' and 'regressive'. Language regression has been reported in 20-47% of children with autistic disorder at a mean age of 18-21 months. Although retrospectively-reported regression has been corroborated by home video analyses, there are no prospective data to characterize this phenomenon.

Objectives: To compare early language trajectories in siblings of children with ASD, with and without parent-reported language regression.

Methods: Language development was assessed prospectively in 189 high-risk infants (siblings of children with ASD) and 85 low-risk comparison infants using the Mullen Scales of Early Learning - Expressive Language subscale (MSEL-EL) at 12, 24 and 36-42 months and the MacArthur Communication Development Inventory (CDI) at 12 and 18 months (direct and parent-report measures, respectively). Language regression was assessed retrospectively by parent report at 36-42 months using the Autism Diagnostic Interview-Revised (ADI-R), defined as loss of at least 5 established communicative words for at least 3 months. Diagnostic outcomes at 36-42 months were determined using the ADI-R, the Autism Diagnostic Observation Schedule (ADOS) and DSM-IV-TR, blind to prior study assessments. ASD symptoms at 12 months were assessed using the Autism Observation Scale for Infants, and at subsequent assessments using the ADOS.

Results: Language regression was reported in no controls, but in 8 siblings at mean age 16.6 ± 4.1 months, including 6 of 20 with autistic disorder (AD; 30%), 0 of 25 (0%) with other ASDs, and 2 of 144 not diagnosed with ASD (1.4%); p<.001. Within the AD group, loss or plateau of skills (decrease or no change in MSEL-EL raw scores between yearly assessments) was observed in 4 of 6 (66.7%) with parent-reported regression, and 2 of 14 (14.2%) without regression (p=.037; Fishers exact test). Language development slowed (based on decline of 1 standard deviation or more in standard scores between assessments) in 6 of 6 (100%) with parent- reported regression, and 7 of 14 (50%) without (p=.051; Fishers exact).

Children with and without parent-reported regression did not differ on language (as indexed by the MSEL and CDI) or non-verbal cognitive scores (as indexed by the MSEL) at 12 months, and had similar ASD symptom severity at all time points. Among the 2 high-risk infants with parent-reported regression who did not receive an ASD diagnosis at age 3, one child, diagnosed with language disorder at 3 years, had no change in MSEL-EL raw score (and a drop in standard scores from 82 to 55) between 12 and 24 months. The second child, who did not have any clinical diagnosis at age 3 years, had MSEL-EL raw scores that increased between 12 and 24 months, and stable/increasing standard scores.

Conclusions: In our prospective high-risk cohort, parents of 30% of children with AD reported language regression a the 3-year assessment. There is some agreement between retrospective and prospective measures of language regression, but trajectory patterns overlap, suggesting that 'early' and 'regressive' onset in AD might occur on a continuum that includes developmental slowing or plateau, as well as frank regression.

126.01 Preverbal Vocalizations in Infant Siblings of Children with ASD. R. Paul*, A. Klin and K. Chawarska, *Yale University School of Medicine*

Background:

Prelinguistic vocal behavior is known to be related to speech development in typical children (Oller, 1999; McCune & Vihman, 2001). However, prelinguistic behavior has been shown to be atypical in preschoolers with ASD (Sheinkopf et al., 2000), and expressive language delay is a nearly universal feature of the development of children with ASD (Tager-Flusberg et al., 2005).

Objectives:

The present study examined prelinguistic vocal behavior in infants at high risk for developing ASD as a result of having older sibling diagnosed with ASD, and compared these to vocalizations of infants at low risk for ASD, who did not have a diagnosed sibling. Our aim was to determine whether infants at risk for ASD show delays or differences from typical development in terms of their production of speech sounds, syllable structures, and prosody in the prelinguistic period. Such differences, if identified, could be useful in early identification of high risk children who are in the greatest danger of developing ASD or related disorders.

Methods:

Subjects were drawn from those participating in a longitudinal study of behavior and development of infant siblings of children with a diagnosis of ASD. As part of participation in the longitudinal study, infants are seen at at least four time points during the first year of life. At each visit standard assessments of behavior and development, as well as data from experimental tasks were collected. The present report presents cross-sectional analysis of vocal productions collected at the 6, 9, and 12 month visits. Vocal samples were audiorecorded during a five-minute free-play mother-child interaction, in which mothers were presented with quiet toys, asked to play with their baby and to attempt to encourage the baby to vocalize. Cross-sectional vocalization data from twenty children in each of the two diagnostic groups were analyzed at each of the three visits. Analyses included:

Consonant inventory (Shriberg & Kwiatkowki, 1994)

Syllable structure level (Olswang et al., 1987)

% Canonical syllable production (Oller, 1998)

Atypical prosodic productions (Sheinkopf et al., 2000).

Analyses were completed by two trained raters with experience in phonetic transcription who were blind to participants' age and risk status. Point-to-point reliability for ratings was over 80%.

Results:

There were no between-group differences in vocal behavior at six months. At nine months, high risk infants, as a group, produced fewer canonical syllables, fewer consonant types, less mature syllable structures, and more atypical prosody than those in the low risk group. By twelve months, only differences in prosody persisted. The high risk group appeared to have "caught up" in terms of sound and syllable production with their low-risk peers.

Conclusions:

These findings suggest that infants at high risk for ASD do show differences from low risk peers in vocal production at certain points in the first year of life. These differences may be helpful, in conjunction with other measures, in clarifying risk status. In addition, the suggestion of delay in prespeech development seen in these data may contribute to understanding the trajectory of expressive language acquisition in ASD.

126.02 Group Level Similarities and Differences in Neural Processing in Infants at Genetic Risk for Autism: Implications for Developing Predictors of Later Behavioral Outcomes. M. Elsabbagh*[1], E. Mercure[1], H. Garwood[1], A. Volein[1], L. A. Tucker[1], K. Hudry[2], S. Chandler[2], K. Frame[2], T. Charman[2], S. Baron-Cohen[3], P. Bolton[4] and M. Johnson[1], (1)*Birkbeck, University of London*, (2)*Institute of Education, University of London*, (3)*University of Cambridge*, (4)*Institute of Psychiatry*

Background: Despite a considerable number of studies focusing on the early behavioral phenotype in infants at-risk for autism, very little is known about potential differences at the level of brain processing. Most studies focusing on overt behavioral manifestations have found only subtle differences in infants at-risk compared to control groups within the first year of life, but the differences in the subgroup that goes on to develop autism becomes increasingly clear over the second year. On the other hand, some findings suggest that reliable differences in neural processing may be present within the first year.

Objectives: The aim of the study was to examine the neural correlates of face and gaze processing in a large group of infant siblings of children diagnosed with ASD (Sibs-ASD) compared to a control group with no family history of autism (control). Another aim was to explore how neural components could be used as predictors of the later emerging phenotype in the second year of life, through focusing on preliminary data from a small subset of cases followed longitudinally.

Methods: One hundred infants (50 sibs-ASD and 50 control) aged six to ten months were recruited for the study. Event-related potentials were recorded while infants viewed dynamic images of females displaying direct or averted gaze. Face stimuli were also compared with visual noise generated from the same faces.

Results: Relative to the control group, the sibs-ASD group showed both similarities and differences in the amplitude and latency of components related to face and gaze processing. The groups did not differ in early components related to perceptual processing but they did differ in some of the later components. Moreover, the differences do not appear to be driven by a few atypical infants in the sib-ASD group.

Conclusions: As a group, infant siblings of children with autism show differences in a number of components related to neural processing of face and eye gaze. Preliminary results from follow-up of a subset of infants in the risk group will be used to draw implications for how these early ERP differences at the group level could be mapped onto individual behavioral outcomes at two years of age, using a battery of standardized behavioral measures. The need for developing individual and continuous measures of both predictors and outcomes will be emphasized.

126.03 Infants at High Risk for Autism Spectrum Disorder: Social-Communication and Language Skills at 12 Months. S. Macari*, K. Bearss, G. Gengoux and K. Chawarska, *Yale University School of Medicine*

Background: Infants who have an older sibling with Autism Spectrum Disorder (ASD) are at risk for early social and communication difficulties, including language delays and ASD.

Objectives: To compare 12-month-old infants at high risk for ASD (HR-SIB) and infants without genetic liability for ASD (low risk, LR) on measures of verbal and nonverbal development as well as their social-communicative functioning. The toddler version of the ADOS (ADOS-T; Lord et al., 2008) is designed for toddlers ages 12 to 30 months and quantifies delays and abnormalities in communication, social interaction, and presence of repetitive behaviors.

Methods: 35 HR-SIB infants and 26 LR infants were assessed at 12 months with the Mullen Scales of Early Learning and the ADOS-T by psychologists blind to infants' risk status. Verbal and Nonverbal DQ scores were derived from the Mullen Scales. Two indices were obtained from the ADOS-T: A subset of 14 items comprises the Social-Affective/Restricted Repetitive Behavior (SA/RRB) algorithm (range=0-28), and the Joint Attention (JA) algorithm (Gotham et al., 2007) includes 5 items (range=0-10). The diagnostic status of HR-SIB infants was still unknown at the time of this submission.

Results: Language abilities of the HR group were significantly lower (Mullen VDQ mean=80.4,

SD=18.0) than those of the LR group (VDQ mean=91.4, SD 17.5), but there were no group differences on nonverbal scales. VDQ was negatively correlated with ADOS-T scores both in the LR group (r=.55, p<.001) and in the HR group (r=.40, p<.05). ADOS-T SA/RRB algorithm scores were significantly higher (denoting more atypical presentation) in the HR-SIB group (mean=12.0, SD=5.7) compared to the LR group (mean=8.5, SD=4.1). Furthermore, on the JA algorithm, the HR-SIB group also scored higher (mean=5.9, SD=2.8) than LR infants (mean=3.9, SD=1.7). The group differences on algorithm scores were not attributable to a few infants with extremely high scores. Analysis of algorithm items showed that HR-SIBs engaged in significantly fewer showing behaviors, were less likely to respond to joint attention bids, and directed fewer vocalizations and facial expressions to others than LR infants. Exploration of other ADOS-T items revealed that infants in the HR-SIB group were less likely to respond to a playful tease, spent less time maintaining/directing parents' attention, and had less developed functional play skills than the LR infants. There were no group differences on restricted and repetitive behaviors.

Conclusions: Results suggest that compared to low-risk infants, infants at high risk for ASD demonstrate less robust early-emerging social-communication skills. Delays in both nonverbal social communication and language skills were evident by the first birthday. In both low-risk and high-risk infants, lower verbal DQ scores were associated with social/communication difficulties measured by the ADOS-T. The findings suggest that, as a group, high-risk 12-month-old infants demonstrate vulnerabilities in domains of social interaction, communication, and verbal ability. We are currently in the process of collecting data at 24 months on the entire cohort at which point we will examine the predictive validity of performance at 12 months with regard to diagnostic outcome and overall levels of social, communication, and language development.

126.04 Differential Early Temperament Trajectories in Children at High Risk of Developing Autistic Spectrum Disorder. N. Garon*[1], J. Brian[2], W. Roberts[3], I. M. Smith[4], P. Szatmari[5], L. Zwaigenbaum[6] and S. E. Bryson[4], (1)*IWK Health Centre*, (2)*Hospital for Sick Children & Bloorview Kids Rehab*, (3)*University of Toronto*, (4)*Dalhousie University/IWK Health Centre*, (5)*McMaster University*, (6)*University of Alberta*

Background: The heterogeneous nature of Autistic Spectrum Disorder (ASD) has posed an ongoing challenge for attempts aimed at identifying core neuropathological mechanisms. To date, limited progress has been made in identifying subgroups that are reliably distinguished by course of the disorder, response to treatment or prognosis/outcome. One promising approach to understanding the heterogeneity in ASD is the study of temperament. Individual differences in temperament have been documented in samples of children with ASD (Sutton et al., 2003), and in high-risk 2-year-olds subsequently diagnosed with ASD (Garon et al., 2008).

Objectives:

The main objective of the present study was to determine whether differences in clinical course (as indexed by age of onset and severity of symptoms) are associated with distinct early temperament trajectories.

Methods:

Infant siblings of children with ASD were assessed prospectively at 6 and 12 months on the Infant Behavior Questionnaire (IBQ) and at 24 months on the Toddler Behavior Assessment Questionnaire (TBAQ), both completed by parents. At 36 months, an independent 'gold-standard' diagnostic assessment for ASD was conducted. Two temperament factors, *reactivity to the environment* and *distress*, found previously to be associated with ASD (Garon et al., 2008) were used in the present analysis. Scores on these temperament factors were analyzed using a linear mixed model with age (6, 12 and 24 months) and subgroups (defined by onset and severity of ASD symptoms) as the independent variables.

Results:

Three distinct early temperament trajectories distinguished subgroups within the high-risk infant sibling cohort. Among those diagnosed with ASD, children with earlier and more severe symptoms were distinguished by a profile of strikingly low reactivity to the environment from 6 months of age onward coupled with a dramatic increase in distress between 6 and 24 months. While their temperament was more stable over time, children with later and less severe symptoms were distinguished by a profile of high

distress from 6 months of age onward coupled with a gradual decrease in reactivity to the environment between 6 and 24 months. Children in the sib group who were not diagnosed with ASD had higher than normal reactivity from 6 months of age onward combined with higher than normal distress from 12 months onward. Finally, at 12 months, even after co-varying ASD symptoms, children in the sib group who were low on both environmental reactivity and distress (flat affect) at 12 months experienced the largest decrement in IQ between the ages of 12 and 24 months.

Conclusions:

The present findings suggest that early temperament trajectories may provide insights into the heterogeneity of ASD beyond that provided by traditional diagnostic approaches.

126.05 Temperament Profiles of Infants Subsequently Diagnosed with ASD. M. Del Rosario*[1], T. Hutman[1], G. S. Young[2], S. J. Rogers[3], S. Ozonoff[2] and M. Sigman[1], (1)*University of California, Los Angeles*, (2)*M.I.N.D. Institute, University of California at Davis Medical Center*, (3)*M.I.N.D. Institute, University of California at Davis*

Background: Parent reports of child temperament differentiate children with an Autism Spectrum Disorder (ages 3-8) from typically developing children. Children with ASD tend to be less adaptable, less persistent, and less responsive than typical children (Hepburn and Stone, 2006). In a longitudinal study of infants at risk of developing ASD, those who developed ASD were rated by their parents as more passive than low-risk controls at 6 months, and were more persistent/less distractible in their visual attention to objects at 12 months (Zwaigenbaum, Bryson, Rogers, Roberts, et al., 2005).

Objectives: To examine the temperament profiles of infants who are subsequently diagnosed with autism and to compare these profiles with those of typical children and high-risk children who do not meet criteria for ASD.

Methods: Infants with an older sibling with ASD (n=132) were compared to children with no family history of autism (n=97) at 12 months of age. A subset of the 12-month sample was also seen at 6 months (high-risk: n=98, low risk: n=86). Temperament ratings of children who met criteria for ASD at 36 months (n=20) were compared with those of unaffected high-risk children and with low-risk controls. The Carey Temperament Scales (McDevitt & Carey, 1996), a parent-report questionnaire, were administered at both the 6- and 12-month time points. ASD diagnoses were conferred at 36 months based on the ADOS-G (Lord, Risi, Lambrecht, Cook, et al., 2000) and clinicians' best estimates.

Results: Parent reports regarding child temperament differed between diagnostic groups. 6-month-old infants who were subsequently diagnosed with ASD were rated higher on both the Adaptability and Mood subscales of the Carey Temperament Scales than low-risk controls. These scores indicate slower adaptation to environmental changes and more negative affect, respectively. The same patterns persisted at 12 months. Furthermore, infants who were subsequently diagnosed with ASD were ranked lower on the Distractibility Subscale at 12 months. Infants in the affected group were less adaptable, less distractible, and more negative in affect than typical children. Mean scores on the Carey subscales were compared between groups using independent samples t-tests. All p values were less than 0.05.

Conclusions: Temperament profiles differentiate children with autism and neurotypical children by 6 months of age. These temperament patterns may be early analogues of later manifestations of autism. They are likely to have a negative impact on children's social opportunities. Temperamental profiles may be useful in identifying children at heightened risk for ASD.

Oral Presentations Program
127 Imaging - Medical Implications?

127.00 Patterns of Epileptiform Activity in Autism as Revealed by MEG. J. D. Lewine*, M. Stein, C. Demopoulos and M. Stepansky, *Alexian Brothers Medical Center*

Background: It is well established that children with an autism spectrum disorder (ASD) are at higher risk for developing clinical seizures than the general population, with 25-30% reported to have epilepsy by the time they reach adolescence. Interestingly, many children with autism who do not have clinical seizures are nevertheless reported to have epileptiform EEG examinations. Current clinical guidelines for the evaluation of children with autism indicate that EEG is warranted whenever clinical seizures are suspected or there is a regression in language skills. We have previously demonstrated that EEG

reveals epileptiform activity in >45% of sedated autistic children with a history of regression, whereas simultaneous MEG reveals epileptiform activity in >60%, with the increased sensitivity for MEG mostly reflecting MEG's superior ability to detect activity within the upper bank of the superior temporal gyrus.

Objectives: The current study sought to better define MEG and EEG patterns of epileptiform activity in autism, especially with respect to other clinical factors including gender, presence of clinical seizures, intelligence, level of language function, and regressive versus developmental delay language profiles.

Methods: Forty minutes of whole-head MEG and simultaneous EEG data were collected from more than 80 sedated children (ages 3-16) diagnosed with autistic disorder (DSM-IV, ADI-R, ADOS). MEG data were collected using a 306 channel biomagnetometer system equipped with both planar gradiometers and magnetometers. EEG data were acquired with 19-60 electrodes configured in an augmented 10-20 array. Sedation was achieved with either oral clonidine and chloral hydrate, or IV propofol, as needed. The MEG and EEG data were analyzed for epileptiform transients with multiple dipole modeling used to characterize the origins of individual discharges.

Results: Although less that 15% of the children had a history of clinical seizures, MEG revealed epileptiform activity in >60%. Epileptiform abnormalities included isolated spikes and sharpwaves, and also sharp burst discharges. Perisylvian activity was more commonly seen than activity in other brain regions, but most children showed a multifocal, bihemispheric profile of epileptiform abnormalities. For approximately 20% of the children with an abnormal MEG, the simultaneous EEG was within normal limits. This pattern was most commonly seen for children with MEG abnormalities restricted to the superior temporal plane. Contrary to initial expectations, epileptiform activity was NOT more prevalent in children with history of language regression than those with the more typical pattern of developmental delay (early-onset) autism. Low functioning children were twice as likely to show epileptiform activity as high functioning children, but the severity of autism per se, was not a significant factor. Children that were verbal but without functional language were more likely to show epileptiform abnormalities than children that were high functioning or children that were completely non-verbal.

Conclusions: MEG reveals epileptiform abnormalities in the majority of children with autistic disorder. This activity is most prominent in low functioning children with non-functional language, with the high incidence of peri-sylvian activity suggesting that the epileptiform activity is a direct neurobiological cause or consequence of disordered language circuitry.

127.01 Incidental Magnetic Resonance Imaging (MRI) Findings in Young Children with Autism. D. G. Amaral*[1], C. W. Nordahl[2], T. J. Simon[1], R. L. Hansen[3] and S. L. Wootton-Gorges[4], (1)*University of California, Davis*, (2)*M.I.N.D. Institute, University of California at Davis*, (3)*University of California at Davis*, (4)*University of California, Davis Medical Center and U.C. Davis Children's Hospital*

Background: Data on incidental MRI findings in young children is only recently beginning to be seriously evaluated (Kim et al., 2002). Despite the fact that there have been a number of MRI studies of very young individuals with autism, there have been no reports on the rate of incidental findings encountered in these studies. Interestingly, polymicrogyria and macrogyria have been reported in adults with autism (Piven 1990). In the context of a large scale MRI study of young children (2-4-years-old), we have encountered several incidental findings. We have endeavored, therefore, to more systematically evaluate the occurrence of incidental findings in our study sample.

Objectives: To evaluate the rate of significant incidental MRI findings in young children (2-4-years-old) with autism relative to typically developing controls.

Methods: Structural MRIs have been acquired in 107 children (73 autism spectrum disorders [ASD], 34 typical development [TD]) ages 27-56 months (mean 40 months). Exclusionary criteria were limited only to those with a contraindication for MRI. Retrospective clinical evaluations of the MRI scans have been carried out by a pediatric neuroradiologist blind to subject diagnosis.

Results: Significant incidental findings occur at a higher rate in children with autism spectrum disorders than in typically developing controls. Examples of significant incidental findings include

Dandy-Walker Syndrome variants, ventriculomegaly, Chiari I malformations, and global cortical atrophy. We will present types and statistical evaluations of the occurrence of incidental findings of all children in this ongoing MRI study.

Conclusions: Incidental findings with significant clinical implications have been detected in a larger proportion of children with autism than in age-matched typically developing children. This raises the prospect that there may be clinical benefit to conducting routine MRIs in children diagnosed with autism.

127.02 Normal Rates of Clinical Neuroradiological Abnormalities in Children with High Functioning Autism. R. Vasa*[1], M. E. Richardson[2] and S. H. Mostofsky[1], (1)*Kennedy Krieger Institute, Johns Hopkins University School of Medicine*, (2)*Kennedy Krieger Institute*

Background: Magnetic resonance imaging (MRI) brain scans have been used to analyze highly specific volumetric and morphological features of the brains of people with autism, however there have been no comprehensive studies on the rates of basic clinical neuroradiological abnormalities identifiable in MRI scans.

Objectives: To examine the rates of clinical neuroradiological abnormalities in children with HFA, comparing them with the rates for typically developing (TD) children and a clinical control group comprised of children with Attention-Deficit/Hyperactivity Disorder (ADHD).

Methods: Clinical radiological reports based on MRI brain scans were collected for 87 children with HFA (12 girls), 168 TD children (79 girls) and 125 children with ADHD (47 girls), 7.21-13.85 years old. These subjects were recruited as part of an ongoing neuroimaging and behavioral study; children with a history of epilepsy or known genetic diagnosis were excluded from participation. Findings were categorized as normal or abnormal, with 13 abnormal sub-categories defined. Three-way chi-square analysis was used to compare the within-group rates of normal versus abnormal reports and the incidence of each abnormal sub-category with a usable number of subjects. The abnormal sub-categories analyzed were asymetrical ventricles, Chiari I malformation/low-lying tonsils, cystic lesions, focal subcortical signal abnormalities, focal white matter signal abnormalities, heterotopia, mega cisterna magna/posterior fossa cyst and mild ventricular prominence/volume loss.

Results: Three-way chi-square analysis revealed no significant effect of group on the overall rate of clinical neuroradiological abnormalities (X^2 = 2.06, p = 0.36); percentages of children in each diagnostic group with reported neuroradiological abnormalities of any type were HFA: 10.3%, TD: 12.5% and ADHD: 16.8%. Analyses of individual sub-categories of abnormalities revealed a significant group difference for mega cisterna magna/posterior fossa cyst (X^2 = 7.51, p = 0.02); reported percentages in each group were HFA: 1.2%, TD: 0.0%, ADHD: 4.0%. Post-hoc two-group comparisons revealed that this result was not related to autism-associated differences, but rather to a higher rate of mega cisterna magna/posterior fossa cyst in children with ADHD compared to TD children (X^2 = 6.84, p = 0.009).

Conclusions: The lack of significant differences in rates of clinical neuroradiological abnormalities in children with HFA, TD children and children with ADHD suggests that anatomical abnormalities attributable to diagnosis are more subtle than what is seen at the level of clinical MRI examination. Implications for routine use of clinical MRI scanning in children with HFA will be discussed.

127.03 Neuroradiological Incidental MRI Findings in Children with Autism Compared to Healthy Typically Developing Controls. S. J. Spence[1], A. W. Buckley*[2], M. Gozzi[1], R. K. Lenroot[1], L. S. Clasen[1], J. N. Giedd[1] and S. E. Swedo[2], (1)*NIH*, (2)*National Institute of Mental Health, National Institutes of Health*

Background: Autism is a complex neurodevelopmental disorder that is likely due to many different etiologies. Comprehensive medical work-ups reveal pathology in only a small fraction of cases (5-10%). Brain imaging yield is usually reported to be low. In fact, the Practice Parameter for autism from the American Academy of Neurology does not recommend routine imaging.

Objectives: As part of an ongoing comprehensive phenomenological investigation designed to determine meaningful subtypes of autism, structural brain MRI is performed on all subjects. We compared results from the autism (AUT) subjects to a typically developing control group (TYP) to determine if there are more neuroradiological findings in autism.

Methods: Autism diagnosis was confirmed with the ADI-R, ADOS and clinical judgment. Structural brain MRI was performed using a 1.5T scanner in 69 autistic children (12 females, 57 males; mean age 4.5, sd 1.37) and 53 typically developing children (12 females, 41 males; mean age 4.7, sd 1.37). There were no significant differences between groups for age and gender. AUT subjects were scanned while sedated and TYP scans were done during natural sleep or while awake. All studies were read by NIH staff neuroradiologists for clinical purposes. Clinical reports were then reviewed and categorized as follows: unequivocally normal; normal but with some variant mentioned in the report; possibly abnormal but of unclear clinical significance; or definite pathology with clinical relevance.

Results: The rate of definite pathology was not significantly different between groups and was low overall: 1/53 (2%) in TYP children (1 with intraparenchymal cystic lesion) and 2/69 (3%) AUT children (1 with an intraparenchymal cystic lesion and 1 with cortical dysplasia). Rates of unequivocally normal and normal variants were also not significantly different between groups: 67% and 12% respectively in the AUT group and 77% and 17% in the TYP group. Normal variants including mild cerebellar ectopia, prominent perivascular spaces, or mega cisterna magna were seen in both groups. However, the rate of possible abnormalities was significantly higher in the autistic children than the controls (Fisher's Exact, p=.01) with 13/69 (19%) AUT showing a questionable abnormality (5 with some white matter findings, 3 with evidence of old insults, 3 with developmental changes, 1 with large arachnoid cyst, and 1 with a circulatory abnormality) compared to 2/53 (4%) TYP (1 old insult and 1 developmental change).

Conclusions: Compared with typical controls, autistic children had similar rates of clinically relevant structural abnormalities as well as normal scans and non-clinically relevant normal variants. However, the rate of possible abnormalities was higher in the group with autism. The significance of these findings is unknown. One possible limitation of the data is that the neuroradiologists were not blind to diagnosis. A second blinded reading is being done to ensure that there were no biases in the interpretation of the AUT group. However, if these represent true abnormalities in this subset of patients, further investigation into their meaning may provide clues to the clinical presentation and/or etiopathogenesis of autism.

127.04 Sound Sensitivities in Autism: Evaluation by MEG and Treatment by AIT. J. D. Lewine*, C. Demopoulos and M. Stepansky, *Alexian Brothers Medical Center*

Background: Despite the fact that 40% of children with an ASD appear to show sound hypersensitivities, essentially nothing is known about the relevant neurobiology. Nevertheless, there are numerous anecdotal reports that some music-based therapies can alleviate sound sensitivities and provide a general improvement in autistic features. Of particular interest is the Berard method of Auditory Integration Training [AIT] which involves listening to 10 hours of specially modulated music. Recent reviews of AIT universally conclude that there is a lack of scientific data to support or discourage its use for children with autism, but many children still receive AIT, often at considerable expense.

Objectives: This study sought to explore the neurobiology of sound sensitivities and document the possible efficacy of AIT in autism.

Methods: Twenty-two high functioning subjects with an ASD participated in psychophysical and MEG evaluations. During initial interview, ten of these subjects did not self-report sound sensitivities, whereas twelve did. Ten normal comparison subjects were also evaluated. During psychophysical testing, subjects were presented with 5 trials of 250, 2000, and 5000 Hz tones of variable loudness [40, 60, 70, 80, or 90 dB], and on each trial the subject was asked to rate the sound as soft, comfortable, loud, or uncomfortably loud. MEG was then used to obtain average evoked responses to 100 presentations of each pitch tone at 75 dB. Dipole modeling was then used to characterize the amplitude of the M100 response in each hemisphere and a laterality index was computed. All subjects with reported sound sensitivities subsequently underwent AIT, with 3 month follow-up psychophysical and MEG evaluations.

Results: Subjects without sound sensitivities demonstrated average uncomfortable loudness levels [UCL] at 86 dB, with no differences between the control and ASD group without sound sensitivities. For both of these subject groups, individual laterality indices on the MEG were all between -0.25 and +0.25. For each ASD subject with sound sensitivities, UCLs were below 80 dB in

at least one of the frequency categories, with tones below 80 dB frequently reported as uncomfortable. On MEG, there were two distinct sub-populations of sound sensitive subjects. Five subjects showed laterality indices within the normal range for all pitches, whereas 7 subjects had indices with absolute values of >0.5 for at least one pitch Following AIT, the 5 subjects with normal indices at baseline failed to show any significant improvements in UCLs or changes in laterality indices. In contrast, subjects with highly asymmetric MEG auditory response profiles at baseline showed improvements in UCLs of 5-10 dB, and a reduction of laterality indices into the normal range.

Conclusions: A subset of subjects with ASDs and sound sensitivities show abnormal auditory processing profiles characterized by an imbalance in auditory response between the two hemispheres. For these subjects, AIT appears to decrease sound sensitivities and normalize auditory processing profiles. For sound sensitive subjects with normal MEG profiles at baseline, AIT is not effective, presumably because they have a different neurobiological basis for their sound sensitivities.

127.05 Noradrenergic EFFECTS on Functional Connectivity in Autism. A. Narayanan*[1], C. White[1], S. Saklayen[1], M. Scaduto[1], A. Abduljalil[1], P. Schmalbrock[1] and D. Q. Beversdorf[2], (1)*The Ohio State University*, (2)*University of Missouri, Columbia*

Background: Previous experiments have demonstrated decreased functional connectivity in subjects diagnosed with ASD when compared to controls, during language tasks. Therefore, drugs that affect functional connectivity may be beneficial in ASD. Noradrenergic antagonists have shown benefit for individuals with ASD in a semantic network flexibility task. The noradrenergic system is upregulated in stress, which causes a decrease in the flexibility of access to semantic networks, resulting in decreased performance in individuals without neurodevelopmental diagnoses under stress. This impairment in the network flexibility due to stress is reversed by administration of centrally acting β-adrenergic antagonists. Propranolol (a central and peripheral β-blocker) has also shown benefit for language and social behavior in ASD.

Objectives: We wished to determine whether administration of propranolol would increase functional connectivity observed during language tasks in ASD as compared to nadolol (peripheral-only β-blocker), administered to control for effects on peripheral blood flow.

Methods: Subjects with ASD and age and IQ-matched controls without neurodevepmental diagnoses were scanned using a Philips 3T scanner, while instructed to respond to the pronunciation (phonological) of a word related to a cue word in a block-design task. Data was preprocessed and analyzed using SPM5 and the correlation of time series was calculated and compared between drug conditions.

Results: Administration of propranolol revealed a significant main effect of increased functional connectivity between activated brain regions across all brain region pairs as compared to nadolol. Effects on heart rate and blood pressure were identical between the two drugs. These results reveal an increase in functional connectivity upon administration of propranolol in ASD that is not attributable to peripheral blood flow effects.

Conclusions: This may suggest an anatomical substrate for the effects of noradrenergic agents on tasks involving a network search within the brain.

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128.01 1 Sleep Modulates Daytime Behavior in Children with Autism Spectrum Disorders. S. E. Goldman*, K. Adkins, K. L. Surdyka and B. A. Malow, *Vanderbilt University*

Background: Sleep problems are highly prevalent in children with autism spectrum disorders (ASD) and contribute to problematic daytime behaviors. Studies employing objective measures of sleep in relation to parent report of sleep and daytime behavior have been limited.

Objectives: We hypothesized that parental sleep concerns in children with ASD, confirmed by objective measures of sleep, would modulate daytime behavior in specific, rather than global, dimensions.

Methods: Fifty eight children, ages 4–10 years, participated in this study. Forty-two had a clinical diagnosis of ASD confirmed by the Autism Diagnostic Observation Schedule, and were defined as ASD-PS (n = 27) or ASD-GS (n = 15) based on the Parental Concerns Questionnaire. Sixteen were typically developing (TD) and

reported to be good sleepers. Behavior was measured by the Childhood Behavior Checklist (CBCL), Repetitive Behavior Scale (RBS), and Parental Concerns Questionnaire (PCQ). Sleep was measured with two nights of wrist actigraphy (Mini-Mitter AW64) and polysomnography (PSG); nights were averaged. Measurements obtained included total sleep time (TST), sleep latency (SL), sleep efficiency (SE), wake time after sleep onset (WASO), nighttime movement and fragmentation (MFI)-actigraphy only, and arousal index (AI)-PSG only. Kruskal-Wallis statistics were used to determine significance between all three groups, and Mann-Whitney U tests provided between group comparisons on the overall significant parameters with significance set at $p < 0.05$.

Results: On the RBS, the ASD-PS group showed significantly increased scores on the compulsive scale as compared to the ASD-GS group. On the PCQ, the ASD-PS group showed more hyperactivity than the ASD-GS group. Both the ASD-GS and ASD-PS groups differed significantly from the TD children globally on the CBCL, RBS, and PCQ, with the exception of the sleep item on the PCQ. The groups differed on objective measures of sleep. With actigraphy, the ASD-PS group differed significantly from the ASD-GS group on sleep latency [mean(SD)] [53.4(25.6) versus 23.0(19.0) minutes]; sleep efficiency [80.9(6.6) versus 88.3(5.1)%], and MFI [(12.5(3.4) versus 9.4(3.1)]. With PSG, the ASD-PS group differed significantly from the ASD-GS group on sleep latency [(54.0(41.7) versus 34.9(34.3)] minutes. The ASD-GS and TD children were comparable on sleep parameters, except that the TD children had a higher MFI [(14.0(3.3) versus (13.5(3.4)].

Conclusions: Our results suggest that poor sleep in children with ASD, as defined by objective parameters, selectively modulates compulsive behavior and hyperactivity, as measured by parent report. Defining the phenotype of sleep in ASD, and its relation to daytime behavior, provides the foundation for focused studies of pathophysiology and targeted interventions.

128.02 2 Differentiated Effects of Sensory Interventions on Aberrant Behavior and Sleep Patterns in Children with Autism. G. R. Mancil and M. Boman*, *Kelly Autism Program at Western Kentucky University*

Background: The complexity of the central nervous system is abstract; yet, neuroscientists demonstrate evidence that sensory input evokes physiological changes in the body (Ben-Sasson et al., 2008). Sometimes we observe these changes in persons who seem to react strongly to everyday sensory input, particularly individuals on the autism spectrum who generally have more frequent and intense reactions to external sensory stimuli. A person with autism spectrum disorder (ASD) typically has trouble processing information from the outside world because sensory problems literally make it difficult to understand what is being seen, heard, and touched. Although the severe reactions to various external sensory stimuli have been discussed in the literature for decades (Baranek, Wakefield, & David, 2008), there is little to no empirical evidence or systematic interventions to address the sensory problems. Objectives: Determine the effectiveness of sensory related interventions on aberrant behavior and sleep patterns in children with ASD. Methods: The subjects were referred by a local autism center that provides services for children with autism spectrum disorder and their parents. The subjects' diagnosis of ASD was confirmed by a review of records and the completion of the ADI-R. Aberrant behavior and abnormal sleep patterns were confirmed by direct observations conducted independently by two data collectors. Interviews and direct observation measures previously developed by the authors were used to determine appropriate interventions for the aberrant behavior and abnormal sleep patterns. Following the identification, an alternating treatment design was utilized to show a functional relation to the identified intervention compared to other interventions (Kennedy, 2005). The researchers trained data coders to collect data who were blind to the study. Results: The sensory interventions identified through the interviews and direct observations demonstrated differentiated effects on aberrant behaviors of the subjects. That is, the identified sensory interventions were the only interventions that resulted in the aberrant behaviors reducing to and remaining at zero. Further, as evidenced by the differentiated effects in the alternating treatment design, sleep patterns improved for the subjects. Conclusions: Findings of this study show the utility of a systematic interview and direct observation measures in identifying sensory interventions to decrease aberrant behaviors and improve sleep patterns of individuals diagnosed with ASD.

128.03 3 The Influence of Caregiver Verbal Interactions during Conjoint Consultation on Child Outcomes. A. A. Smith*, A. Kirk and L. A. Ruble, *University of Kentucky*

Background: Public schools are facing increasing pressure to serve a growing number of students with autism using research supported practices. One research supported practice that has promise as a feasible and sustainable intervention is conjoint consultation. Consultants, who have both expertise in autism and skills in consultation, may play a critical role in addressing the unmet needs of children with autism through supporting their parents/caregivers and teachers. Research is lacking on caregiver involvement during conjoint consultation for students with autism. Also lacking is information on what types of caregiver verbal interactions predict child outcomes. This information can inform the processes of consultation important for child outcomes.
Objectives: To characterize caregiver verbal interactions during conjoint parent-teacher consultation. To prospectively examine the influence of caregiver verbal interactions on child outcomes (i.e., attainment of IEP objectives).
Methods: A randomized controlled study of parent-teacher consultation and outcomes was conducted. The experimental group consisted of 18 children between the ages of 3 and 8 years, their teachers, and their caregivers. The teacher and caregiver participated in a 2.5 hour COMPASS consultation (Ruble & Dalrymple, 2002). Consultations were audiotaped and transcribed. The functional purpose of the speech acts used by caregivers during the consultation will be coded using the Psychosocial Processes Coding Scheme (PPCS; Leaper, 1991). Items include quality of involvement (distancing vs affiliative) and type of influence (direct vs indirect). Reliability of the segmenting (using percent agreement) and coding (using kappa) will be determined. The predictive variables will be the types of verbalizations of caregivers. The dependent variable will be child goal attainment of IEP objectives using Goal Attainment Scaling rated by an observer who was unaware of the child's group assignment, IEP, and teaching plans. Standard multiple regression analysis will be applied.
Results: The results will be determined following data analysis and be available for the upcoming IMFAR meeting.g
Conclusions: Parent and teacher consultation is a realistic and feasible approach for improving the outcomes of children with autism. Very little research, however, is available on the effectiveness of consultation and even less on the process of consultation. Understanding what caregiver behaviors are important for consultation outcomes will help inform models of consultation that encourage those parent behaviors.

128.04 4 Differences in Perceptions of Mothers and Fathers of Children with Autism in Regards to Stress, Family Cohesion and Adaptibility. S. A. Donaldson*[1], J. H. Elder[1], J. Kairalla[2], G. Valcante[3], R. Bendixen[3], R. Ferdig[3], E. H. Self[1], P. J. Mutch[4], T. K. Murphy[4], J. Walker[3], C. Palau[1], M. Serrano[1] and T. Galante[3], (1)*College of Nursing*, (2)*Unviersity of Florida*, (3)*University of Florida*, (4)*University of South Florida*

Background: Literature indicates that mothers and fathers of children with autism report higher levels of stress than parents of children with other developmental disabilities. Literature also indicates that mothers typically experience higher levels of stress than fathers. In our 4-year NIH-funded study focused on teaching fathers skills to help increase social interaction and communication in their children with autism, an important question is whether father and mother stress levels and perceptions of family cohesion and adaptability differ prior to receiving the training intervention.

Objectives: To determine whether differences exist in perception of stress, family cohesion and family adaptability between mothers and fathers of children with autism.

Methods: As part of our 4-year on-going NIH-funded study, we analyzed baseline data from 21 families and compared mother and father scores from the Parental Stress Inventory (PSI) and the Family Adaptability and Cohesion Scale II (FACES II). Descriptive statistics and paired t-tests were used for each of the three scores to describe and statistically test whether pre-intervention differences existed between mothers and fathers in families having a child with autism.

Results: Both mothers and fathers scored at or above the 90th percentile on the PSI indicating clinically significant stress levels. Comparisons of the mother and father PSI scores did not show a statistically significant difference ($p=0.10$), although mothers averaged 9.6 points higher on the PSI scale (99.5 to 89.9). An analysis of the FACES II scores indicated both mothers and fathers perceived their family's cohesion as being "connected" with no statistically significant difference reported between fathers and mothers ($p=0.16$; mother mean: 68.0, father mean: 65.1).

Statistical analysis of the family adaptability scores indicated highly significant differences between mothers and fathers (p=0.0008; mother mean: 50.1, father mean: 45.0); This indicates that the mothers perceived the family as more flexible and less structured than fathers.

Conclusions: Mothers and fathers of children with autism experience clinically significant stress levels. While both parents perceive the family as cohesive, fathers view the family as more structured than mothers. These conclusions suggest the need for interventions that address the stress that both parents of children with autism experience. Further, because there were differences between fathers and mothers, there may be a need to design interventions that address these differences, as well as the similarities.

National Institute of Nursing Research, National Institutes of Health

128.05 5 Stress and Positive Emotions among Mothers of Children with Autism Spectrum Disorder: a Daily Diary Study. N. Ekas* and T. L. Whitman, *University of Notre Dame*

Background: Raising a child with autism spectrum disorder (ASD) is typically a challenging and stressful experience for mothers. As a result of these challenges, mothers report greater levels of negative psychological outcomes, including depression and negative affect. Previous research suggests that positive affect may serve as a moderator of the relationship between stress and negative outcomes.

Objectives: To investigate the relationship between daily stress and daily negative affect, using a daily diary methodology, among mothers of children with ASD. A second purpose is to explore the role of daily positive affect as a possible moderator of these relationships.

Methods: Participants consisted of 49 mothers with a child with ASD. Mothers completed the following questionnaires on a daily basis for 30 consecutive days: Positive and Negative Affect Scales (PANAS-PA; PANAS-NA), Daily Negative Life Events Scale, and Daily Autism-Related Stress Scale.

Results: Analyses revealed that daily negative affect was associated with daily life stress ($r = .67$, $p < .001$) and daily autism-related stress ($r = .43$, $p < .01$). In addition, daily positive affect was also associated with daily negative affect ($r = -.27$, $p < .05$). Simple linear regression analyses also found similar results. Results of moderation analyses found that the interaction of daily life stress and positive affect was significant ($B = -.027$, $p < .05$), but the autism-related stress and positive affect interaction was non-significant. Multilevel modeling using Hierarchical Linear Modeling software will be conducted to confirm these preliminary findings.

Conclusions: Findings confirm that daily stress predicts daily well-being among mothers of children with ASD. Specifically, higher levels of both life and autism-related stress predict higher levels of negative affect. Further, we also found that positive affect can help buffer the negative effects of stress. Mothers who report high levels of stress and high levels of positive affect have lower levels of negative affect as compared to those who report high levels of stress and low levels of positive affect. These findings suggest that incorporating positive experiences into daily living may be beneficial for families.

128.06 6 Outcomes for Families of Children with Autism Spectrum Disorder Involved in Early Intervention. S. Mastrangelo*, *York University-Milton and Ethel Harris Research Initiative*

Background: The importance of family outcomes is broadly acknowledged in the literature (Bailey, et al, 2006) however there is skepticism and confusion about typologies of outcomes, how they should be measured, and their usefulness in early intervention. A family outcome is defined as a benefit experienced by families as a result of services and supports received. It is also what happens as a result of services provided by families to their children with autism spectrum disorder (Harbin & Neal, 2004). To date, there is little research on the effects and/or benefits of specific interventions on family outcomes.

Objectives: The purpose of this research was to examine parental perceptions on the effects of DIR/Floortime intervention on family outcomes and to compare this data to a comparison group of parents whose children received community based interventions. I wanted to determine whether the DIR/Floortime early intervention program promoted more positive family outcomes as compared to families whose children received a variety of community based interventions. Other questions that were addressed included: a) What outcomes are the children and families experiencing? and b) how do family outcomes

relate to variations in child and family characteristics and the services provided? The objective was to identify and document the full range of family benefits that might be expecteded from early intervention along with any possible drawbacks. In my comparative analysis of the two parent groups I measured the effects of intervention on specific family outcomes (as outlined in the Autism Spectrum Disorder Family Outcomes Questionnaire, ASDFOQ, a new tool for measuring family outcomes).

Methods: Thirty-eight families from Ontario who are currently involved in a larger DIR/Floortime early intervention study through the Milton and Ethel Harris Research Initiative at York University participated in this study. Parents in both the DIR/Floortime intervention program and community based intervention program rated their perception of family status on a set of outcomes identified in the literature as expected or reported benefits of participation in early intervention upon entry and then after nine months of intervention vis a vis the Autism Spectrum Disorder Family Outcomes Questionnaire. Parents also responded to 3 open ended questions (both pre and post intervention) pertaining to family resiliency which were analyzed qualitatively using NVivo.

Results: Data analyses involved conducting a within and between groups pre and post assessment of family outcomes. Families in the DIR/Floortime group demonstrated more positive family outcomes (with the greatest impact on family quality of life, relationships with family members, and ability to integrate in community activities). Parent perceptions about the child's level of functioning after intervention significantly improved in the DIR/Floortime group with parental reports revealing greater child affect, responsiveness and engagement.

Conclusions: The DIR/Floortime intervention approach (with its focus on parents as the primary interventionists and where the goal is to train parents in strategies to improve the social, emotional and communicative reciprocal relationship) produced more positive family outcomes than families in the comparison group receiving a combination of community based interventions. The findings provide a description of how families are doing overall in outcome areas after exiting early intervention.

128.07 7 Roles and Experiences of Fathers of Children with Autism. D. B. Nicholas*[1], L. Zwaigenbaum[2], P. McKeever[3], R. MacCulloch[4] and W. Roberts[5], (1)*University of Calgary*, (2)*University of Alberta*, (3)*Bloorview Kids Rehab and Hospital for Sick Children/ University of Toronto*, (4)*The Hospital for Sick Children*, (5)*University of Toronto*

Background: It is recognized that families tend to provide the majority of care for children and adolescents with autism. However, what is not well understood is how family care unfolds over the course of development for children with autism and their families. This gap is surprising given that (a) parents play a critical caregiving role, and (b) intervention programming for children with autism often takes place in the home. Addressing this gap is particularly important given that the well-being of parents is paramount if they are to be sustained in their crucial caregiving role. While another study by this team is examining maternal experiences, this study will examine the roles, tasks and experiences of fathers of children with autism and how couples negotiate care for the child. With emerging literature that suggests one member of the family can integrally affect other family members, this study is crucial in understanding the impact of autism in family life. Based on study findings, paternal and family-based supports and interventions can targeted to need and evaluated.

Objectives: To address these gaps, this study addresses the following research questions:

1. How do fathers perceive and experience autism in their children (up to age 25 years)?
2. How do fathers' experience of autism change over time?
3. What are fathers' roles in autism care, and what contributes to fathers' wellbeing in the context of these roles?
4. How do mothers and fathers negotiate and give meaning to their children's disorder and care?

Methods: The study will involve a theoretical sample of 20 fathers of a child with autism. Fathers are participating in a single semi-structured interview. Sample size permits variation in child age and diagnosis, cultural background, and family constellation. Sample

selection is based on population databases of children (birth to 25 years) followed at the Autism Research Units at The Hospital for Sick Children, Toronto and the Glenrose Rehabilitation Hospital, Edmonton, both in Canada.

Results: The presentation will address the following areas of study outcome:

- paternal roles and experiences associated with autism and how they change over time
- tasks that fathers fulfill in caring for their children with autism
- fathers' perceptions of the challenges and blessings associated with childhood autism
- ways that fathers are supported/not supported
- supports that fathers would find helpful in managing their child's care
- ways that parents negotiate care, and ways that parents attribute meaning to their caregiving experience.

Conclusions: The study addresses an existing gap of knowledge and, as targeted resources are developed offering paternal support, practical benefits for fathers and families can result. Based on the identification of paternal experiences and needs yielded in this study, it is anticipated that an ameliorative resource addressing these needs will be developed and tested in a future study within this research program.

128.08 8 Marital Adjustment, Social Support, and Parenting-Related Stress in Mothers and Fathers of Preschool-Aged Children with Autism. T. St. John*, A. M. Estes and J. Munson, *University of Washington*

Background: The associated adaptive, social, and behavioral challenges of autism spectrum disorders (ASD) can impact family adaptability and functioning. Prior research assessing these variables has yielded mixed results, especially regarding marital adjustment. Some studies indicate worse marital adjustment in parents of children with ASD while others find similar levels of marital adjustment compared to controls. Evidence does suggest that parents of children with ASD experience high levels of parenting-related stress. There may be different ways in which marital problems, social support, and parenting stress impact mothers versus fathers.

Objectives: This study aims to (1) determine whether parents of children with ASD report worse marital adjustment and increased parenting-related stress compared with parents of children without ASD, (2) assess the relationship between marital adjustment and parenting stress, (3) assess the relationship between marital adjustment and social support, and (4) compare marital adjustment, parenting stress, and social support in mothers versus fathers.

Methods: Participants were 52 mothers and fathers of children with ASD and 25 mothers and fathers of children with developmental delays without ASD (DD). Mean age of children in the ASD and DD group was 44 months. Data from this study was collected during phase one of a larger longitudinal study that sought to identify early behavioral and biological predictors of outcomes in ASD. Marital adjustment was measured using the Dyadic Adjustment Scale. Parenting-related stress was assessed using the Questionnaire on Resources and Stress. Social support was measured using the Social Support Questionnaire.

Results: (1) Preliminary results suggest that parents in the ASD group report worse marital adjustment and higher parenting-related stress than parents in the DD group. (2) Worse marital adjustment was correlated with higher levels of parenting stress in both mothers and fathers in the ASD group. (3) For mothers in the ASD group, higher social support satisfaction was correlated with better marital adjustment but the relationship between number of supports and marital adjustment was not significant. For fathers in the ASD group, higher numbers of supports and greater satisfaction with these supports was correlated with better marital adjustment. Further analysis will explore the relationship between marital adjustment, social support, and parenting stress, and potential differences between mothers and fathers.

Conclusions: Parents of children with ASD appear to have worse marital adjustment and higher levels of parenting stress compared to parents of children with other developmental disabilities. Higher levels of parenting stress are associated with worse marital adjustment in mothers and fathers of children with ASD. Furthermore, if parents of children with ASD are more satisfied

with their social support they are likely to report better marital adjustment. A greater number of supports appear to be related to better marital adjustment for fathers, but not mothers.

128.09 9 Relationships Between Aberrant Behavior in Children with ASD and Maternal Parent Stress Over Four Years. S. Jull*, P. Mirenda, R. Stock and K. Bopp, *University of British Columbia*

Background: Parents of children with autism spectrum disorders (ASDs) often experience significant stress related to their children's behaviour (Herring, Gray, Taffe, Sweeney & Einfeld, 2006). Typically, "autistic behaviours" such as aloneness and repetitive behaviours are the focus of early intervention. However, these may not be the primary sources of stress experienced by caregivers.

Objectives: This study examined relationships between parent stress and child aberrant behaviour at three time points: at the onset of and exit from early intervention, and after the children attended school for 1-2 years.

Methods: Sixty-five children with ASD were assessed 6 months following the initiation of early intervention (T1), at intervention termination around 18 months later (T2), and 28 months afterward (T3). At T1, children's mean CA was 56 months and 73% were from two-parent families; 83% were males and 53% were European-Canadian. Maternal parenting stress was measured with the Parenting Stress Index (PSI) and child behaviour problems were assessed using the Temperament and Aberrant Behavior Scale (TABS). Negative life events (via the Family Inventory of Life Events, FILE), total social supports (via the Inventory of Social Supports, ISS), and parent coping style (via the Family-Crisis Oriented Personal Evaluation Scales, F-COPES) were also measured. At all three time points, Pearson correlations were calculated between PSI subscales, FILE weighted life event total scores, ISS total scores, and F-COPES coping style subscales. Variables that were correlated with the PSI were then used as controls in partial correlations between PSI subscales and TABS subscales at T1, T2, and T3.

Results: At T1, F-COPES Passive Appraisal (PA) scores were significantly correlated with two subscales in the PSI. With PA partialled out, the TABS Detached and Hypersensitive/Active subscales were significantly correlated with the PSI Difficult Child subscale (r=.36 and .55, respectively). At T2, FILE life events and ISS Total Support scores were significantly correlated with one PSI subscale. With these variables controlled, the TABS Hypersensitive/active subscale was significantly correlated with the PSI Difficult Child subscale (r=.88). The PSI Parent-Child Dysfunctional interaction subscale was also significantly correlated with the TABS Hypersensitive/active subscale (r=.63). At T3, F-COPES Acquiring Social Support (ASS) scores were significantly correlated with the PSI Parental Distress and Difficult Child subscales. With ASS controlled, the PSI Parental Distress subscale was significantly correlated with the TABS Dysregulated subscale (r=.49).

Conclusions: Results indicate that, early in intervention, behaviours in the TABS Detached subscale (e.g., aloneness, stereotypy) and the TABS Hypersensitive/active subscale (e.g., tantrums, irritability) were both related to parental stress. However, as children aged, only behaviours in the latter subscale continued to be related to parental stress, when other sources of stress were controlled. Finally, by age 8.5, Dysregulated behaviours (e.g., excessive crying, sleep disturbances) were the only behavioural subset that continued to be associated with parent stress. This suggests that, beyond the initial stages of intervention, autistic symptomatology may not be the primary source of stress for parents. Service providers should develop targeted interventions to decrease Hypersensitive/active and Dysregulated behaviours when amelioration of parental stress is a goal.

128.10 10 Vaccines & Autism: A Parental Perspective. A. M. Young* and L. A. Ruble, *University of Kentucky*

Background: Highly publicized controversy has arisen regarding the possible links between childhood vaccines and autism in the. As fear of links between vaccination and autism begin to take root, the decision to vaccinate may become increasingly difficult for many parents. In preparation for parents' pending concern, healthcare providers need to thoroughly understand the range of attitudinal and ecological factors influencing parents' intention to vaccinate.

Objectives: The purpose of this study is to explore the perspectives of parents of children with autism regarding childhood vaccination. Attitudinal and ecological influences on vaccine acceptance are assessed. Attitudinal associations include parental

perceptions of vaccine safety/efficacy, parental perception of disease risk, and parental distrust of health providers. Ecological associations include family demographics (income, race, community size, and education), parental exposure to anti-vaccine media, and parental experience with child's medical care.

Methods: A convenience sample of parents of children with autism (n=20) were recruited through their participation in another autism-related study. Two self-administered cross-sectional surveys representing (a) attitudes toward childhood vaccines and (b) perception of medical care were developed. Both surveys were comprised of 4-point Likert scale items ranging from *strongly agree* to *strongly disagree*. The first survey contained 43 items and 4 main subscales (perception of vaccine safety/efficacy, perception of disease risk, communication with provider regarding vaccination, and vaccine acceptance). Vaccine acceptance represented the dependent variable and was measured by responses on a 3-item subscale that asked about parents' general intent to vaccinate and to recommend others to vaccinate. The perception of medical care survey consisted of 23 items and 5 subscale ratings of physicians' informativeness, interpersonal sensitivity, partnership building, communication, and competence, as well as 2 subscale ratings of general accessibility and affordability of medical care. Simple linear regression was used to assess bivariate associations between constructs and vaccine acceptance. Multivariate linear regression with forward selection was used to identify the construct most strongly predictive of vaccine acceptance.

Results: The internal reliability of the two measures was strong, and the Cronbach's alpha exceeded 0.7 for 6 of the 7 subscales entered into all linear regression models as potential predictors. No statistical significance ($p<.05$) was reached in the bivariate associations between vaccine acceptance and media exposure or parental demographics. Similarly, none of the attitudinal variables reached statistical significance in their bivariate associations with vaccine acceptance. The only construct to reach statistical significance in its bivariate association was affordability of care ($p=.028$). The multiple linear regression revealed affordability of care to be the strongest predictor of vaccine acceptance ($R^2=0.401$, $p=.027$).

Conclusions: Attitudes toward childhood vaccination among parents of children with autism can be influenced by a complex array of factors. To effectively communicate with parents regarding vaccination, healthcare providers must recognize the existence of attitudinal and ecological influences, such as affordability of care.

128.11 11 Socioeconomic Status among Utah Children with Autism Spectrum Disorders and Mental Retardation. J. Pinborough-Zimmerman*[1], R. Satterfield[2], S. Hossain[2], D. Bilder[1] and W. McMahon[1], (1)*University of Utah*, (2)*Utah Department of Health*

Background: A number of studies have associated higher social class and maternal education with autism spectrum disorders (ASDs) and lower social class and maternal education with mental retardation (MR).

Objectives: The goal of this study was to examine and compare the socioeconomic status (SES) of children with ASD-only, MR-only, and ASD with MR (ASD/MR), with SES of children from a comparable birth cohort.

Methods: This study utilized the datasets from Utah Registry of Autism and Developmental Disabilities (URADD), Utah Birth Certificate Records and Utah State Tax Commission. The URADD identified children born in 1994 with ASD-only (n=98), MR-only (n= 113), ASD/MR (n=33) and a population-based birth cohort (n=24,361) living in Salt Lake, Davis and Utah counties in 2002. Socioeconomic status was measured using various income indices and level of maternal education. Chi-square, T-tests and ANOVA were computed. The correlation between maternal education, household income, and taxes paid was computed for each study group. Multiple logistic regression models were generated with 95% CI using SAS 9.1.

Results: The four groups were fairly homogeneous across measures of income and tax exemptions in 1994. Mother's of MR cases (MR-only and ASD/MR) were significantly older compared to mothers from the birth cohort (p=.02). However, there was no significant difference across all socioeconomic indicators. Families of ASD-only cases had significantly higher incomes (p=.03 and a net difference of $220) and paid significantly higher taxes (p=.04 and a net difference of $44) than birth cohorts. Mother's of ASD-only cases compared to MR-only cases had significantly higher education (p=.002). There was no

significant difference across all SES indicators between families of ASD/MR cases compared to the birth cohort. Irregardless of income, mothers of ASD-only cases were 1.9 times more likely (p=.03) to have an education above high school.

Conclusions: The ASD-only cases were significantly different on measures of income, taxes paid, and maternal education. Further study is needed to compare socioeconomic variations among children with ASD-only, MR-only, and ASD/MR.

128.12 12 Pivotal Response Training Group Therapy Model: Analysis of Parent and Child Outcomes. M. B. Minjarez*, S. E. Williams and A. Y. Hardan, *Stanford University School of Medicine/Lucile Packard Children's Hospital*

Background: The number of children diagnosed with autism spectrum disorders has increased recently in the United States. With children being diagnosed as young as 18 months of age, the need for services is increasing. Research has demonstrated that interventions based on operant conditioning procedures, such as Applied Behavior Analysis and Pivotal Response Training (PRT), lead to improvements in the core symptoms of autism. This research supports that parents can become effective intervention agents. Historically, such interventions have been delivered to families individually; however, the increase in service demand makes this model relatively inefficient. As a result, researchers are beginning to develop strategies that investigate the effectiveness of group treatment models.

Objectives: The aim of the present study was to demonstrate that parents can learn PRT procedures in a ten-week group therapy format and meet fidelity of implementation criteria for treatment termination typically used in individual therapy. An additional purpose was to demonstrate that when parents learn the PRT procedures their children make correlated gains in language.

Methods: Twelve families have participated to date in this trial and data collection is ongoing. Data were obtained using systematic scoring of parent and child target behaviors observed during 10-minute video-taped parent-child interaction probes. The independent variable was parent participation in a 10-week PRT parent training group. The dependent variables were: 1) parent fidelity of implementation of PRT intervention during parent-child interaction probes, and 2) number of child utterances (number of 10-second intervals containing one or more utterances) used during parent-child interaction probes. These variables were scored by independent raters. Data were collected at baseline, week five of treatment, and post-treatment (week 10). Paired t-tests were used to examine changes in the dependent variables from baseline to week ten of treatment.

Results: Preliminary findings suggest that parents can learn PRT in a group format and their children benefit from it. Specifically, targeted intervention skills not used by parents during baseline parent-child interactions are used at post-treatment (10 weeks), as evidenced by changes in fidelity of implementation scores (Baseline score: 9.3 ± 4.8; Post-treatment score: 20.1 ± 5.4; paired t test: 5.782; df =11; $p<0.0001$). Benefits were also observed in children, who demonstrated an increased number of utterances during a 10-minute parent-child interactions (Baseline score: 27.5 ± 15.5 utterances; Post-treatment score: 40.9 ± 5.3; paired t test: 3.287; df =11; p= 0.007).

Conclusions: Findings suggest PRT strategies can be taught to parents in a group treatment format with both parents and children demonstrating positive outcomes in targeted behaviors. These findings are analyzed in light of the clinical need for more data driven, cost-effective, and efficient treatment models and the research need for more robust analysis of naturalistic behavioral treatment models. Our preliminary findings suggest future controlled studies are warranted using larger samples to further examine the efficacy of this group treatment model and to identify indicators of treatment response.

128.13 13 Promoting Joint Attention for Toddlers with Early Indicators of Autism: a Parent-Mediated Approach. H. Schertz*[1], K. Baggett[2] and S. Odom[3], (1)*Indiana University*, (2)*University of Kansas*, (3)*University of North Carolina*

Background: Joint attention has been demonstrated to be a foundational competency that supports later development of higher level social-communication skills; however, its development is disordered in autism. Intervention models that promote joint attention are needed for implementation during the toddler period when intervention can be most effective. Also needed are early intervention models that follow developmentally appropriate family-centered

approaches for toddlers consistent with recommended early intervention practice. For toddlers with autism who have difficulty with interaction, primary caregivers may have the best chance of eliciting early nonverbal communication successfully. A three-site research project has implemented a manualized intervention, the Joint Attention Mediated Learning (JAML) model that responds to these needs.

Objectives: When performance during and following the intervention period is compared to baseline performance, participants will improve in (a) focusing on faces, (b) turn-taking, (c) responding to joint attention, and (d) initiating joint attention.

Methods: In the first two years of a three-year project, 22 participants participated in the parent-mediated four-phase JAML intervention in a single case experimental research design using a multiple baseline probe across targeted outcomes. Participants entered new phases of intervention as they demonstrated proficiency in preceding phases, showing stable performance above a baseline trend line that was used to predict future performance. Researcher-constructed measures for each targeted outcome were assessed and independently coded from 10-minute video-recordings taken at weekly intervention sessions. The four phases of intervention corresponded to the four targeted outcomes: focusing on faces, turn-taking, responding to joint attention, and initiating joint attention. In a series of systematic paired replications, the study explored variations in frequency of intervention sessions, parents' use of audio-recordings to report child progress, and the use of video modeling and reflection with parents. In addition, the intervention was implemented with one Spanish-speaking and additional bilingual families. Intervention was provided in weekly sessions in which trained interventionists provided individual guidance to parents in their homes. Parents carried out planned and naturally occurring interaction-based activities daily and reported each week on child participation. An intervention manual guided intervention activities and a parent manual presented mediated learning principles and descriptions and examples of activities to promote each of the four targeted outcomes.

Results: To date, across the three sites two participants have progressed through the four phases of intervention (i.e., achieved the four targeted outcomes), seven completed the first two phases, and six completed the first phase. Remaining participants are in the baseline condition. We expect the majority of participants to have ended the intervention before the IMFAR meeting in May, when updated data will be presented. Of those participants who will have completed the intervention we expect that the majority will have achieved all four targeted outcomes.

Conclusions: Experimental results show that joint attention can be achieved by toddlers with early signs of autism using a naturalistic parent-mediated intervention model in which primary caregivers build on their intimate knowledge of their children's preferences for activities and materials to interact with their toddlers in developmentally sequenced stages designed to build toward joint attention.

128.14 14 Observing Autistic Family Relationships: a Pilot Study on Support Intervention to Parents and Their Children. L. Vismara*[1] and G. Doneddu[2], (1)*University of Cagliari*, (2)*A.O.B. (Azienda Ospedaliera Brotzu)*

Background: Recently, some contributions have highlighted the negative effect of parental stress upon the efficacy of interventions oriented towards the child with an Autistic Spectrum Disorder (ASD), who shows increasingly more behavioural problems at the parents' increase of stress level (Osborne et al., 2008).

Objectives: Our study is aimed to assess the efficacy of a psychological support to parents and their children in terms of observed and perceived improvements in the quality of relationships.

Methods: 7 families of children with an ASD (6 males and 1 female; mean chron. age= 7 yrs and 7 month; SD=3 years; mean IQ= 89.83; SD= 27.92) were assessed before and after a supportive intervention through a standardized observational procedure: the "Clinical Lausanne Trialogue Play" used as a measure of the change as regards the family's affective and behavioural functioning. Individual, from 0 (not adequate) to 2 (fully adequate), and family codes, from 0 (fully dysfunctional) to 40 (fully functional) were scored.

Results: At the beginning of intervention, the mean score was 20.14 (s.d. 4.02), within the dysfunctional alliances range; up to now, we found among 4 follow ups a significant difference

(2-tailed paired t test; P= 0.0469; DF= 3) after intervention; the mean increased to 24 (s.d.= 3.65), placing families within stressed but functional alliances. Moreover, the intervention improved the compliance between parents and the professionals involved in the multi-disciplinary care of the child.

Conclusions: the study emphasizes the need to involve personally the parents and to consider their feelings and worries for their child in order to ameliorate the ability to share feelings and to develop inter-subjectivity processes.

128.15 15 Joint Attention Intervention Combined the Training of Children with Autism and Their Parents: The Preliminary Findings. C. H. Chiang*, Y. L. Peng and S. J. Chiang, *National Chung Cheng University*

Background: Joint attention (JA) deficit is one of core symptoms in children with autism. Recent literature demonstrated that the JA intervention could improve their JA, play and language abilities. Few studies explore the efficacy of JA intervention systematically and never include parent training in the program in Taiwan.

Objectives: The purpose of the study was to develop JA intervention program combined child and parent training for children with autism in Taiwan. The current report was to describe initial findings for six children with autism in JA intervention group and 3 children in the controlled group.

Methods: Participants were 9 children with autism (CA = 28-52 months, MA = 17-30 months), diagnosed with DSM-IV-TR and ADOS by a research team including psychiatrists and psychologists. The JA intervention program consisted of two parts, one for children, the other for their parents. The child JA intervention program was referred from Kasari's suggestion (Kasari, et al., 2006). For the child training, each session was 30 minutes, 3 times per week, and the total was 24 sessions. The discrete trial training and milieu teaching approaches were used on the table time and floor time separately. The JA intervention program for the parents was based on the authors' clinical experience and followed the Parent JA Intervention Manual (PJAIM). The first half of the parent training was from session 1 to 12, the interventionist used the PJAIM as a reference to teach the parent what is going on from one way mirror while they are observing his/er child's training session in the play room. From session 13 to 24, the parent was invited to interact with his/er child guided by interventionist for 20 minutes after child's training session. The interventionist assisted the parent to practice the strategies to improve the child's JA skills. The pre-, post-, and 4-month follow-up tests were: ESCS (Mundy, et al., 2003), the structured play (Kasari, et al., 2006), and Reynell Developmental Language Scales (Reynell & Gruber, 1991) and MacArthur-Bates Communicative Development Inventory-Chinese version (Tsao, et al., in press)

Results: The results show that all of the six children improve their JA, play and language abilities after the JA intervention program. For JA, children improve from pointing for requesting an object to showing/giving an object to a person for sharing, and their play skills also improve from child as an agent to multi-schemes for symbolic play in the post-intervention test. The improvements are also shown in the 4 months follow-up test. The parents also changed their teaching strategies from adult-directed approach to child-directed approach in the sessions and maintained the child-directed teaching strategies after 4 month. However, the three children with autism in the control groups seems to develop slow on the three social communicative abilities at post and 4 months follow-up tests.

Conclusions: The initial data revealed that the JA intervention program combining the training of children and their parents is promising. Further studies are needed to recruit more subjects into the two groups to learn the long term effect.

128.16 16 A Strength-Based Approach to Parent Education for Children with Autism. A. Mossman*, *Yale University*

Background: Currently, the vast majority of empirically supported early intervention programs for children with autism include a parent education component. Despite the ubiquitous nature of parent education programs in autism treatment, relatively few studies directly address how parent education should be conducted. The literature on parent variables for parents of children with autism, such as stress and depression, suggest that treatments that facilitate positive adaptation to the child's disability may be beneficial.

Objectives: The purpose of this study was to examine the impact of a strength-based approach to parent education on parent and parent-child

interaction variables.

Methods: An alternating treatments design was employed to compare the effects of therapist statements that highlighted the child's deficits vs. therapist statements that emphasized the child's strengths. These two approaches to parent education were evaluated on the following measures: (1) parent affect following therapist statements, (2) parent statements regarding child behavior, (3) parent affect during parent-child interactions, (4) parent stress during parent-child interactions, (5) parent playfulness, and (6) physical affection.

Results: The results indicate that parents displayed improved affect and decreased levels of stress immediately following therapist statements and during parent-child interactions in the strength-based approach. Additionally, in the strength-based condition, parents demonstrated more playfulness and physical affection toward their child.

Conclusions: Results are discussed in terms of implications for parent education programs, parent well-being, and parent-child interactions.

128.17 17 Practitioners' Disclosure of a Child's Diagnosis of Autism to Parents: Current Practices and Identified Barriers to Effective Communication and Support. D. W. Mruzek*[1], C. Burns[1], E. Baltus-Hebert[1], M. Orlando[1], S. Sulkes[2], J. Yingling[1], K. O'Mara[1], S. A. Nichols[1], L. N. Barzotto[1], M. Ryan[1], D. Vogler-Elias[1], J. Roesser[1] and P. Gemmell[1], (1)*University of Rochester Medical Center*, (2)*Strong Center for Developmental Disabilities, University of Rochester Medical Center*

Background: The disclosure of a diagnosis of autism in children is an event with profound implications for the child and family. Successful disclosure can promote effective and timely understanding of the nature of the disorder, prognosis, and intervention options, and has implications for child and family well-being. Researchers have suggested several factors that are associated with greater parent satisfaction, including interpersonal style of the clinician, quality of the information received, provision of written material, and the opportunity to ask questions. More information about each of these and related areas is needed in order to successfully support and prepare families at the time of diagnosis.

Objectives:

The purpose of this study was to identify professionals' current ASD disclosure practices regarding diagnostic information, related implications, next-step planning, and support for parents' emotional adjustment, as well as their opinions regarding barriers to effective disclosure practice.

Methods: Eighty participants were identified through their membership in one of these four groups: a) the Autism Treatment Network; b) the Autism Special Interest Group of the Association for University Centers on Disabilities; c) the Leadership Education in Neurodevelopmental and related Disabilities network; and d) the University Center for Excellence in Developmental Disabilities network. Participants completed an on-line survey composed of the following sections: Demographics, Background, Description of Current Disclosure Practices, Identification of Barriers to Effective Disclosure, and Recommendations for Effective Disclosure. The survey was meticulously designed after thorough literature review and qualitative data gathered through focus groups. The tool was stringently tested and reviewed for face and content validity by 10 subject matter experts. Participants' responses to the survey were analyzed through quantitative statistical methods (i.e., descriptive statistics, including percent, mean response levels, range of responses, chi-square), as well as qualitative methods (i.e., review and analyses of written responses).

Results: Significant variation was found in how participants reported their practice of autism disclosure to families. A number of variables were identified by participants that contributed to or hampered disclosure of the ASD diagnosis, expectations for outcome, emotional adjustment, next-step planning, and coordination of services.

Conclusions: Results suggest that specific features of the diagnostic setting, clinician's communication style, written information provided, and structure of the diagnostic session significantly impact clinicians' perceptions of and satisfaction with their current disclosure practices. Barriers to effective disclosure were noted in systemic, interpersonal, and content-specific areas.

128.18 18 Parenting Children with Autism Spectrum Disorders: Unique Challenges for Individual and Family Functioning?. M. M. Abdullah*, A. R. Ly, K. Thorsen, S. N. Grondhuis and W. A. Goldberg, *University of California, Irvine*

Background: Impairments associated with Autism Spectrum Disorders (ASD) vary in severity and present unique challenges to parents and families. Previous studies indicate that mothers of children with ASD report higher levels of parenting stress and mental health problems compared to mothers of typically developing children. Research findings regarding differences in marital functioning among parents of children with and without ASD have been mixed with some studies indicating lower levels of marital satisfaction among parents of children with ASD compared to parents of typically developing children and others indicating similar levels of marital satisfaction between the two groups.

Objectives: To examine whether having a child with ASD or not (i.e., diagnostic status) was related to differences in parental well-being, marital quality, and parenting. Poorer parental and marital functioning was expected in families with the added challenges of parenting a child with ASD.

Methods: Fifty-two parents (33 mothers and 19 fathers) participated in a mail-out, mail-back survey study. Participants were predominantly Caucasian, well-educated, and middle- class. Children had been part of a large national study or were seen at a university-based clinic. Twenty-four children had been independently diagnosed with ASD (M=11.17 years, SD=3.23) and 10 children were typically developing (TD) (M=12.00 years, SD=1.58). Independent variables (IVs) were used to differentiate diagnostic groups (DV) and included: (1) parenting pleasure, burden, and importance (Parent Satisfaction Scale; Halverson & Duke, 1991), parenting alliance (Parenting Alliance Measure; Abidin, 1998); (2) marital quality (total score and subscales) (Dyadic Adjustment Scale; Spanier, 1976); and (3) depressive symptoms (Brief Symptom Inventory; Derogatis, 1993).

Results: Diagnostic groups did not differ on demographic variables. MANOVAs and ANOVAs revealed that mothers of children with ASD reported significantly higher levels of depressive symptoms (p=.047) and lower levels of parenting pleasure (p=.031) and alliance (p=.034) compared to mothers of TD children. No significant differences between mothers of children with and without ASD were found for parenting importance, burden, or marital adjustment. When data from both fathers and mothers were aggregated, parents of children with ASD reported significantly lower levels of parenting alliance compared to parents of TD children (p=.030). A logistic regression model including parenting pleasure and alliance was statistically significant, reliably distinguishing mothers of children with and without ASD (p=.026). The full model correctly classified 69.7% of the mothers. When aggregate data were analyzed with parenting pleasure and alliance as IVs, the full model was significant (p=.047) and correctly classified 71.2% of the parents.

Conclusions: Families of children with and without ASD report similar functioning in terms of marital adjustment. However, parents of children with ASD may experience less parenting satisfaction and co-parenting. Moreover, elevated levels of depressive symptoms among mothers of children with ASD warrant further exploration longitudinally and in conjunction with childhood and adolescent developmental outcomes. Although based on a small sample, if replicated, these findings have implications for treatment efforts and support services for families of children with ASD to ameliorate parenting challenges and build on family strengths.

128.19 19 Father Involvement in Families of Children with Autism Spectrum Disorders (ASD). A. R. Ly*, M. M. Abdullah, K. Thorsen, S. N. Grondhuis and W. A. Goldberg, *University of California, Irvine*

Background: Although most family research has primarily focused on the mother-child relationship, a growing literature indicates that fathers make significant contributions to their children's development, independent of the contributions of the mother (Parke, 2002). Beyond needs to include fathers' own perspectives, there is a call for a more contextual research approach. Guided primarily by family systems theory, this study elucidates how the dynamics of the mother-father relationship are associated with the father-child relationship in families with children with ASD.

Objectives: To determine: (1) the extent of agreement between mothers' and fathers' reports of father involvement, (2) whether fathers'

involvement differs between families of children with ASD and families with typically developing children, and (3) whether mothers' beliefs about the fathering role relate to levels of father involvement.

Methods: Forty-nine parents (19 fathers and 30 mothers) participated in a mail-out, mail-back survey. A subsample of 17 mother-father dyads had complete data. The sample was predominantly Caucasian, well-educated, and married. Study children were participants in a larger autism project or were clients from a university-affiliated clinic who received comprehensive evaluations. Measures tapped parental involvement and attitudes toward the fathers' role.

Results: (1) Using intraclass correlations, moderate levels of agreement characterized parents' reports (n = 17) on fathers' involvement in routine child-care (r = .53, p = .01); however, low levels of agreement characterized parents' reports on father involvement in educational activities (r = .12, p = .31). (2) An independent samples t-test (n = 49) revealed fathers in families with and without a child with ASD did not differ in their level of routine child-care [t(47) = -.73, p = .33] or educational involvement [t(47) = 0.91, p = .93]. Mothers undertake approximately 70% of work in both domains. (3) In aggregate analyses (n = 49), parental views endorsing greater importance of the fathering role were associated with greater father involvement only in routine child care (r =.30, p = .04). Analyses restricted to dyadic data (n = 17) showed mothers' beliefs regarding the importance of the fathering role were not significantly associated with fathers' self-reported involvement in either child-care [r = .39, p = .12] or education [r = .14, p = .58]. There was 73% power to detect a large effect size.

Conclusions: Fathers' involvement has been largely overlooked in research in families with children with ASD. The two groups of families were more similar than different; in both, parental views about the fathers' role were related to fathers' level of involvement in routine care and education. The stressors presented by raising children with ASD may fall within average ranges of functioning (Trute et al., 2007). Although underpowered to find small-moderate effects, findings from the current study suggest that the challenges of raising a child with ASD do not appear to lead to fathers being any more or less involved compared with fathers without an affected child. In both samples, mothers are doing the lioness' share of care.

128.20 20 Parent Emotion Coaching and Emotion Regulation in Children with Autism Spectrum Disorders. D. Rezendes* and A. Scarpa, *Virginia Tech*

Background: Emotion coaching refers to the ability of the parent to use emotional situations to help his or her child label the emotions, validate the emotional experience, problem-solve how to deal with these emotions, and/or understand the emotions. There is a growing literature examining the positive effects of emotion coaching on children's ability to develop emotion regulation skills. However, to date, this research has focused exclusively on typically developing children. Due to the emotion regulation difficulties of children with Autism Spectrum Disorders, emotion coaching may provide an effective way for parents to improve emotion regulation skills in their children diagnosed with an Autism Spectrum Disorder.

Objectives: To examine the influence of maternal emotion coaching on child emotion regulation skills

Methods: Mothers were recruited from local and national autism groups, and were directed to a website where they completed the measures online. The Emotion Regulation Checklist (ERC) was used to assess maternal perception of emotion regulation skills in children. The emotion coaching subscale of the Parent Emotional Styles Questionnaire (PESQ) was used to assess self-reported use of emotion coaching.

Results: Data were collected from 127 mothers of children diagnosed with an Autism Spectrum Disorder. Regression findings indicated that maternal emotion coaching was positively associated with child emotion regulation skills, F (1, 128) = 5.255, p = .024. Increases in the use of an emotion coaching parent style in mothers predicted better emotional regulation skills in children.

Conclusions: Results indicate that greater use of maternal emotion coaching is related to improved child emotion regulation skills in children with Autism Spectrum Disorders. It is unclear whether or not parent emotion coaching is directly

affecting child emotion regulation or whether children with better regulatory skills create interactions in which parents can draw from more emotional resources. It is also not clear if these results generalize to fathers. Future research should further examine the potential benefits of emotion coaching on the development of emotion regulation in children with Autism Spectrum Disorders.

128.21 21 Factors That Influence the Psychosocial Wellbeing of Siblings of Children with An Autism Spectrum Disorder Compared to Siblings of Typically Developing Children. S. K. Dickson*[1], K. M. Lesko[1] and J. Pinto-Martin[2], (1)*University of Pennsylvania School of Nursing*, (2)*University of Pennsylvania*

Background: Autism Spectrum Disorders (ASDs) affect 1.5 million Americans and their families. The diagnosis of an ASD has a significant impact on all members of the family; however, few have investigated the relationship between an autistic child and their typically developing sibling. Sibling interviews and parent questionnaires were used to elicit information about how the sibling relationship is affected when one child has an ASD. These findings may have important implications for clinical care of the family.

Objectives: The purpose of this study is to evaluate the effect of having a sibling with an ASD on the psychosocial wellbeing of the typically developing sibling. The specific aims of the study include:

1) to compare the experiences of siblings of children with an ASD to that of siblings of children with a developmental disability (DD) and siblings of typically developing children (TYP);

2) to describe the unique challenges faced by children with an autistic sibling.

Methods: This study integrates both parent and sibling perceptions of the relationship through semi-structured interviews and the Child Behavior Checklist for Ages 6-18 (CBCL).

Results: 131 siblings between the ages of 5 and 16 participated in the study (48 ASD, 49 DD, 34 TYP). The average age of the responding sibling was 10.5 years (ASD), 9.8 years (DD), and 10.1 (TYP). Gender distribution among the groups was nearly even (49% male ASD, 47% male DD, 49% male TYP). Preliminary analysis revealed no significant differences between groups on the mean CBCL subscores and all averages were within the clinically normal range. Although internalizing and externalizing behaviors were significantly correlated to "total problems" across all groups, the degree of correlation varied by group. Similarly, overall "total competence" was not significantly different between the groups; however, the effect of activities, social and school scores on competence varied by group.

Qualitative responses from semi-structured interviews are being coded for analysis. Interview questions examined topics such as: dynamics of sibling relationship, effect of sibling relationship on friendships, household responsibilities, sibling community involvement and experience of different emotions (i.e. guilt, sadness, anxiety, etc.). Analysis of the sibling interviews could highlight some unique challenges faced by ASD siblings with respect to these topics.

Conclusions: This study highlights the need to expand intervention and treatment of ASDs, as well as other developmental disorders, to include a family-based approach. This information is critical for health care providers working with families with a child on the autism spectrum in order to provide the proper anticipatory guidance. Additionally, understanding the various roles held by siblings can inform inclusive support services for the family and thereby improve overall quality of life for diagnosed children.

128.22 22 Family Support Program for Parents of Adolescents and Adults with High-Functioning Autism and Asperger Syndrome in Japan. M. Tsujii*, *Chukyo university*

Background: In Japan, there are many autistic people who have secondary mental disease, and they had been improperly treated based on cultural problems. In Japan, usually single adults live with their families and have been close relationship between parents and autistic adults even in adulthood.

Objectives: The purpose of this study was to reveal an effect on the program for parents of adolescents and adults with High-functioning Autism(HFA) and Asperger syndrome(AS) in Japan. The programs were focused on treatments for Secondary mental, emotional and behavioral problems for adults with HFA and AS.

Methods: The participants were 10 mothers for adults with HFA and AS. We organized two groups for them, and the program was composed with 5 sessions; understanding traits of Autistic people, understanding Secondary mental emotional and behavioral problems, understand mother-child interaction, understanding herself, and how

mother response positively for their child's behavior. Mothers discussed each other in group settings. Their behaviors in daily-life and belief of mothers were evaluated each session and after programs using self-reports of mothers. we assessed mother's change using Parenting Questionnaireionare and child's behavioral changes using Vineland Adative behavior Scales

Results: In the program, mothers could notice their parenting styles depending on Japanese traditional ways and that style could not match their children's autistic traits. Also they could understand their negative response for their children's behaviors, because of difference from standard Japanese way of behaviors. Mothers could learn how to response positively for behaviors of their children and Children's behaviors gradually changed, especially anger expression decreased.

Conclusions: This program encouraged parent's understanding of belief and behaviors for themselves. It is important to notice mothers' traditional beliefs that every adult should do "Normal" behaviors and autistic behaviors should response negatively. It is also important to treat cultural problems for support parents of adults with HFA and AS.

128.23 23 Parents of Preschool Children with ASD: Stress, Burnout, Social Support and Beliefs in ABA during Initial Workshop Training. M. N. Gragg*, D. D. Barrie and M. G. Simmering, *University of Windsor*

Background: There is considerable research supporting the effectiveness of Applied Behavioural Analysis (ABA) for improving the intellectual, social, emotional, and adaptive functioning of children with Autism Spectrum Disorders (ASD). The demand for ABA treatment is high; consequently many families are assigned to wait-lists for intervention. Starting ABA at younger ages is important for positive outcomes for children with ASD, thus, finding alternative ways for parents to access treatment for their children earlier is critical. Many parents want training to implement ABA with their own children, thereby providing behavioural interventions earlier. There has been some concern that intensive ABA training may be too stressful for parents. Alternatively, ABA training may have a positive impact on parents, providing benefits such as feelings of empowerment, increased social support, and reduced stress.

Objectives: To assess levels of stress, burnout, social support, and beliefs in ABA of parents/caregivers of preschool children with ASD as they attend a 2-day workshop on ABA.

Methods: Participants attended a 2-day ABA workshop at a preschool ASD treatment centre as part of a larger study on intensive 3-month parent ABA training. Participants were 14 parents/caregivers of preschool children with ASD (79% mothers), with a mean age of 31.7 years (range 26 – 60). Most had some college education or more (64%), and average family income was $57,000 (Canadian). Their children (92% boys) ranged in age from 34 to 43 months; 9 had diagnoses of ASD and 5 were highly suspected of ASD. All children were on wait lists for ABA, although some were receiving speech therapy or day care. Participants completed measures on stress, burnout, social support, empowerment, beliefs in ABA effectiveness, social desirability, and demographics.

Results: Four parents reported experiencing high stress, while 10 parents reported average stress levels. Two parents were at the burnout/very serious burnout level, 7 parents reported danger signs of burnout, and 5 parents were at a very low level of burnout. Most parents reported being satisfied in often receiving enough social support from family, other parents of children with ASD, and professionals. Twelve parents reported above average levels of empowerment. Thirteen of the 14 parents reported very high beliefs in the efficacy of ABA.

Conclusions: Some parents attending a 2-day workshop on ABA reported high levels of stress and burnout, although most felt satisfied that they had adequate social support and believed highly in the effectiveness of ABA. Attending a 2-day workshop on ABA is an initial step for parents as they seek treatment for their children. It is important to find effective ways to combine training in ABA and support for parents to reduce stress and burnout as they wait for treatment for their preschool children with ASD. Parents who participated in this study will be followed as they wait for intervention, complete a 3-month ABA training program, and implement ABA at home with their children.

128.24 24 An Exploration of the Internal Working Models of Caregiver Attachments in High-Functioning Children with Autistic Disorder. F. K. Chandler*[1] and C. Dissanayake[2], (1)*Olga*

Tennison Autism Research Centre, School of Psychological Science, La Trobe University, (2)*La Trobe University*

Background: Previous research has investigated attachment relationships in children with autism during early childhood, with few differences found from matched control groups. However, little is known of the attachment relationship with the primary caregiver during the period of middle childhood (ages 8-12).

Objectives: The aim in this study was to establish if there are any differences in the internal working models of the attachment relationship in children with High-Functioning Autism (HFA) compared to typically developing (TD) children in terms of overall attachment security, as well as individual components of this relationship. A secondary aim was to establish whether caregivers' perceptions of their child's attachment to them matched their children's own reports. Finally, the relationships between children's performance on theory of mind and memory tasks and attachment security were explored.

Methods: A group of 12 children with HFA and 12 TD children were matched on verbal and overall mental age and chronological age. Children were administered the Kerns Security Scale (KSS; Kerns, Aspelmeier, Gentzler & Grabill, 2001; Kerns, Klepac & Cole, 1996) and the Inventory of Parent and Peer Attachment - Revised (IPPA-R; Armsden & Greenberg, 1987; Gullone & Robinson, 2005), and caregivers completed the same questionnaires from the view point of their child. Children also completed a higher-order theory of mind task and an episodic memory task.

Results: There were no significant differences between the groups in the children's reports of their attachment security, or on the subscales of trust, alienation, communication (IPPA-R), dependency or availability (KSS). In the HFA group, there was a large correlation between children's and caregiver's ratings on the KSS (r = .65). Theory of mind performance in children with HFA was highly correlated with their reports of attachment security as measured by the IPPA-R (r = .86), and moderately correlated with their reports of attachment security as measured by the KSS (r = .34). Episodic memory performance in children with HFA was highly correlated with their reports of attachment security as measured by the IPPA-R (r = .58), and moderately correlated with their reports of attachment security as measured by the KSS (r = .30).

Conclusions: The results support findings from studies of younger children with autism, showing that children with HFA can and do develop secure internal working models of attachment during middle childhood, and that theory of mind and episodic memory abilities may facilitate this development.

128.25 25 Developing An Intervention to Improve Flexibility in High-Functioning Children with ASD: What Do Parents, Teachers, and Children Say They Need?. K. Kane, J. L. Sokoloff, L. Kenworthy and L. G. Anthony*, *Children's National Medical Center*

Background:

Inflexibility is a commonly observed associated feature of high-functioning autism spectrum disorders (HF-ASDs). Although social functioning is the central area of impairment for children with HF-ASDs, it is likely that inflexibility contributes to these social difficulties and impacts them in other areas of functioning as well. Interventions aimed at improving flexibility are limited and not commonly implemented in home and school settings. We are developing an intervention to improve flexibility in students with HF-ASDs, and as a first step in developing this intervention, we wanted to incorporate stakeholder input into the appropriate targets and methods for the project.

Objectives:

We sought to determine the areas of functioning that inflexibility affects in these children's lives, as well as the extent of this impact. Additionally, we sought to learn from parents, teachers and youths with ASD what they have found helpful in improving flexibility, in order to help us determine what factors are critical to developing an intervention targeted at improving their flexibility.

Methods:

We conducted focus groups with four groups of participants: Parents of children and adolescents with ASDs (11 participants), public school special education teachers and staff members (6 participants), special education teachers and staff members in an Asperger's program at a private school (12 participants), and school aged students within the previously mentioned program (17 participants). Questionnaires rating the role of

flexibility in various areas of a child's functioning and the participants' experiences with resources that seek to improve flexibility in this population were collected from all participants.

Results:

In speaking with these groups and analyzing the collected data, we discovered several common themes regarding flexibility, and learned that inflexibility negatively impacts the social, emotional, behavioral, and academic functioning of children. When asked how it feels when he has to be flexible, one student stated: "Like I'm a lobster slowly being submerged into boiling water and I'm about to explode." All participants acknowledged that teaching flexibility skills was crucial, but the groups reported needing a structure for teaching the skills and an active reward system to make the work achievable. Based on questionnaire results, 55% of these teachers rated flexibility as impacting their students socially very often, and 39% of teachers rated flexibility as impacting the students academically very often. Seventy-seven percent of all adult participants rated having flexibility techniques in the classroom as essential, and 73% of these participants rated such techniques as likely being useful in other settings as well. Fifty percent of teachers rated themselves as being very likely to use a flexibility manual in their classrooms if available. Children rated various techniques in terms of their helpfulness, and suggested other options that they thought might help them be flexible.

Conclusions:

Results of questionnaires indicate that inflexibility negatively impacts children with HF-ASDs in multiple areas of functioning. Our findings that a majority of parents and teachers believe that inflexibility impairs social and academic functions in HF-ASD, and that they need specific guidance and resources to intervene in this area, has implications for future intervention research.

128.26 26 The Relationship Between Child-Related Stress of Parent Participants and Child Gains in a Behavioral Intervention Program for Children with Autism Spectrum Disorders (ASD).
R. Gutierrez*[1], S. Dufek[1], L. Schreibman[1], A. Stahmer[2], R. L. Koegel[3] and L. K. Koegel[3], (1)*University of California, San Diego*, (2)*Rady Children's Hospital*, (3)*University of California, Santa Barbara*

Background:
Parents of children with ASD have been shown to have higher stress levels than parents of children without disabilities (Baker-Ericzen et al., 2005). Studies also show that child-related stress may be mediated by parent education (e.g., Koegel, Bimbela, & Schreibman, 1996).
Objectives:
To examine the effect of a behavioral intervention parent education program on various areas of parent stress as measured by the Parenting Stress Index (PSI; Abidin, 1995).
Methods:
Parents of children (aged 2-4 years) with ASD were trained in one of two naturalistic teaching strategies, Pivotal Response Training (PRT, N=20) or the Picture Exchange Communication System (PECS, N = 19). Parents completed the Parenting Stress Index (PSI) before and after intervention. The PSI is a questionnaire that evaluates stress in the parent-child relationship along two scales, one scale focuses on *parent-related* stress (stress due to issues unrelated to the child, such as financial stress or divorce) and the other scale focuses on *child-related* stress (stress due to the child, such as a disability). Child participants received a comprehensive battery of cognitive, language and adaptive behavior assessments before and after intervention. Changes in child-related stress on the PSI were analyzed using analyses of variance by intervention group. After the analyses, for each statistically significant subscale parents were grouped based on whether their stress decreased or did not decrease over the course of intervention. Children were then compared by group (parental decreasing stress or no decreasing stress) using ANOVA to determine whether there were any differences across groups in outcome.
Results:
No differences in stress level or changes in stress were found between the intervention groups (PECS;PRT), therefore data were collapsed across groups for subsequent analyses. No *parent-related* stress scales changed substantially over time. On the *child-related* stress scales, the *Child Reinforces Parent* subscale of the PSI showed a statistically significant decrease overall from pre- to post- intervention. In this analysis, two groups of parents emerged: Group 1 demonstrated decreasing stress over time and Group 2 demonstrated no decreasing stress over time. Changes in child-related parent stress on this subscale were related to child gains in adaptive

social behaviors in our sample, in that child participants in Group 1 showed greater improvements after intervention than child participants in Group 2.
Conclusions:
Although some aspects of child-related stress are positively affected by parent education, parents may need additional support to mediate parent-related stress and a majority of types of child-related stress. Despite the complexity of addressing social deficits in children with ASD, gains in child adaptive social behaviors may be most important in mediating child-related stress in parents of children with ASD. Autism service providers should consider these findings when developing intervention programs for young children with ASD.

128.27 27 Effects of a Family-Based Treatment on the Repetitive Behaviors of Children with Autism. B. Boyd*[1], S. McDonough[2], T. N. Holtzclaw[3] and J. Bodfish[4], (1)*FPG Child Development Institute*, (2)*University of North Carolina*, (3)*University of Alabama*, (4)*University of North Carolina at Chapel Hill*

Background: An important issue in autism intervention research is whether interventions truly impact the core deficits that are presumed to mediate abnormal behavior and development in autism. Recent controlled trials of joint attention and symbolic play interventions have demonstrated that these types of focused interventions can significantly impact core social communication symptoms (Kasari et al., 2006). To date, focused interventions have not been developed for the other primary symptom area of restricted repetitive behaviors. Repetitive behaviors in autism significantly peak during the critical early childhood period when rapid neurological change is occurring. For this reason one can hypothesize that early intervention may be both more effective in terms of immediate impact and also more far-reaching in terms of broader aspects of optimal brain and behavioral development. While pharmacologic options for treating or managing repetitive behaviors have been identified, their safety and utility with very young children with autism have not been established. Because of pathogenic and phenomenological similarities between the repetitive behaviors found in Obsessive-Compulsive Disorder (OCD) and those found in autism (Rapoport & Inoff-Germain, 2000), it is reasonable to ask if behavioral treatments for the former disorder can be translated to treat the latter. Exposure response prevention (ERP) is an evidence-based intervention routinely used to treat repetitive behaviors in OCD.

Objectives: To modify and translate a family based ERP (F-ERP) therapy to treat repetitive behaviors in autism, and examine the effects of the intervention.

Methods: Six participants (ages 2 – 5) diagnosed with an autism spectrum disorder and one of their caregivers participated in the 12-week treatment. The ADOS was used to confirm diagnosis and participants were screened to ensure severity of repetitive behavior using the PDD-CYBOCS (a psychometrically-valid measure). Each enrolled caregiver selected two repetitive behaviors to treat, and then participated in weekly, clinic-based sessions. Caregivers were trained by a therapist using live coaching and modeling. Single case methodology was used to investigate the effects of F-ERP on repetitive behaviors in autism, as it allows experimental control to be established with small N studies. Naïve behavioral raters coded intervention sessions post-hoc to examine treatment effects.

Results: Preliminary descriptive data for 4 of 6 participants show decreasing levels of child repetitive behavior across the 12 week period, and maintenance of treatment gains at a 1 month follow-up home visit. In addition, the findings are replicated for both therapist- implementation of treatment as well as caregiver-implementation. At the conference, single subject graphs will be shown for all 6 caregiver-child dyads to convey participant data and effect sizes will be reported.

Conclusions: Evidence-based behavioral treatments for repetitive behaviors in OCD can be modified and translated to treat repetitive behaviors in young children with autism. Preliminary evidence suggests that F-ERP can be used as an early, intensive behavioral intervention to treat the broad range of repetitive behaviors found in autism. In addition, caregivers of children with autism are able to successfully learn the intervention strategies and implement them in the absence of therapist support (i.e. in home vs. clinic).

128.28 28 Social Functioning and Restricted and Repetitive Behaviors: An Early Analysis of Data from the Autism Center of Excellence and Simons Simplex Collection Studies at UIC. M. Huerta*, R. Loftin, J. Klaver, P. Cali, C. W. Brune and E. H. Cook, *University of Illinois at Chicago*

Background:

Although social skills deficits and restricted and repetitive behaviors (RRBs) are defining features of autism spectrum disorders (ASDs), relatively little is understood about the relationship between them. Recently, it has also been argued that the relationship between RRBs and social engagement has been exaggerated and that these domains are independent (Mandy & Skuse, 2008). Yet, in a recent study of children with ASD, mild social impairment was significantly linked to the presence of more severe RRBs, specifically "insistence on sameness" behaviors (Richler, Huerta, Bishop, & Lord, under review). Further, response to social interventions suggests that a relationship may exist between social engagement and RRBs (e.g., Oke & Schreibman, 1990; Pierce & Schreibman, 1997; Loftin, Odom, & Lantz, 2007).

Re-examining the nature of restricted and repetitive behaviors (RRBs) may shed light on the relationship between RRBs and social communication behavior. Factor analyses of restricted and repetitive behaviors have revealed two subtypes of RRBs: 'repetitive sensorimotor' (RSM) behaviors and the other of 'insistence on sameness' (IS) behaviors (Cuccaro et al., 2003). More recently, a study by Lam, Bodfish, and Piven (2008) identified a 3rd factor of circumscribed interests. Using such an approach to examine RRBs types in children with ASD may be useful to uncover links between RRBs and social functioning.
Objectives: This study will explore the relationship between social functioning and RRBs in individuals with ASDs.

Methods: Subjects will include approximately 49 verbally fluent individuals, ages 5-12 years, participating in genetic studies of autism. Diagnoses of ASD will be confirmed and dimensions of functioning will be measured by the Autism Diagnostic Interview-Revised (ADI-R), the Autism Diagnostic Observation Schedule (ADOS), the Repetitive Behavior Scale-Revised (RBS-R) and the Social Responsiveness Scale (SRS). The relationship between social functioning and RRB will be explored, using age and IQ as covariates.
Results: Results of the data analysis described above will be presented. Implications for ASD treatment and research will be discussed.
Conclusions: These results will add to our existing knowledge of restricted and repetitive behaviors and their relationship to social functioning in children with ASD.

128.29 29 A Clinical Trial of Occupational Therapy for Sensory Dysfunction in ASD. R. Schaaf*[1], T. Benevides[1], D. Kelly[2], E. Blanche[3] and Z. Mailloux[4], (1)*Thomas Jefferson University*, (2)*Children's Specialized Hospital*, (3)*University of Southern California*, (4)*Pediatic Therapy Network*

Background: This paper reports on a study of the effectiveness of occupational therapy strategies to reduce sensory dysfunction and enhance adaptive behaviors and participation for children with ASD and their family. Unusual responses to sensation or sensory dysfunction (SD) are extremely prevalent (80-90%) in individuals with Autism Spectrum Disorders (ASD), contributing to the maladaptive behavioral profile of these disorders and limiting participation in daily life activities. Children with ASD exhibit SD in many ways including self stimulating behaviors, avoiding behaviors (such as placing hands over ears in response to typical levels of auditory input), sensory seeking behaviors (twirling, chewing, etc) and/or "tuning out" behaviors such as not responding to their name or other environmental sensory cues. Families report that SD significantly restricts full participation in daily activities and consequently, interventions to address SD are among the most often requested services (Mandell, et al, 2005; Green, et al, 2006). Despite this, data supporting interventions to specifically address SD are sparse and lack evidence to support their efficacy. This study presents preliminary data on the feasibility, acceptability, safety and efficacy of a manualized occupational therapy intervention for SD for children with ASD ages 5-8 years.

Objectives: Evaluate the feasibility of an intervention protocol that utilizes evidence-based, theory- driven occupational therapy strategies designed to address SD in ASD.

Methods: We follow Smith, et al's (2007) model for systematically validating and disseminating an intervention for ASD in a sequence of steps beginning first with case studies to determine the feasibility of the protocol and its acceptability by families, then moving to fidelity testing and outcome validity in a small controlled trial, and finally a randomized clinical trials to test efficacy under controlled conditions. This paper reports on phase 1: descriptive case studies to address questions of feasibility, acceptability and safety.

Quantitative and qualitative data are obtained pre, mid and post intervention from parents and therapists; and the child's progress toward individual goals is obtained using goal attainment scaling. Other outcome measures include the Sensory Profile to evaluate change in SD; the Vineland to measure change in adaptive behaviors, and participation and quality of life scales.

Results: Qualitative and quantitative data are reported on a range of important and clinically relevant questions such as: Is the manualized intervention viable for children with ASD and SD (feasibility)? Is it acceptable to parents? Is it practical and acceptable to offer the intervention at the stated frequency with supplemental parent education? Which measures best detect meaningful outcomes? Are therapists able to deliver the intervention in a way that is in keeping with its principles (fidelity)? Does the intervention decrease maladaptive sensory behavior, improve adaptive behaviors, improve the family quality of life, and result in greater participation in self care routines, play, and community activities by the child and family?

Conclusions: Data to guide "best practice" for children with ASD and SD are shared and implications for phase 2 and 3 of this project are discussed.

128.30 30 Visual Sensitivity to Angry Point-Light Walkers Varies as a Function of the Observer's Autistic Traits. M. D. Kaiser* and M. Shiffrar, *Rutgers University*

Background: Previous research has shown that typical adults demonstrate an "anger superiority effect" in their heightened visual sensitivity to potentially threatening human actions. For example, typical adults are more sensitive to the presence of angry human gaits than to the presence of happy, fearful, sad, or neutral gaits. The visual perception of emotional human motion depends upon the Superior Temporal Sulcus and the amygdala. Autism is associated with anatomical and functional abnormalities in these "social brain" areas. This suggests that the anger superiority effect may be modulated by observers' autistic traits.

Objectives: Do typical adult observers vary in their visual sensitivity to emotional gaits as a function of their autistic tendencies?

Methods: Twenty-three participants were recruited from the Rutgers student body. They completed the Autism-Spectrum Quotient (AQ) questionnaire that measures the magnitude of autistic traits in typical adults with normal intelligence. Then participants completed a psychophysical task. Emotional human gaits were depicted in point-light movies. Each point-light walker displayed anger, happiness, fear, sadness, or a neutral emotional state and was hidden within a cloud or mask of identically moving points. On half of the trials, the starting locations of the points defining the walker were scrambled so that the walker was "absent." Participants viewed each masked point-light movie for 3 seconds and reported with a button press whether a walker was "present" or "absent" in the mask. Emotion was neither mentioned nor explicitly judged.

Results: AQ scores fell in the expected normal range (Mean = 17.35, SD = 4.69). A median split of AQ scores divided participants into low and high AQ groups. Each group's performance on the psychophysical task was analyzed as the mean D-prime for each emotional gait. D-primes were computed by subtracting the standardized rate of false alarms from the standardized rate of hits. Overall, walker detection performance was best with angry walkers. However, there was a significant effect of AQ group on visual sensitivity to angry walkers ($F(21,1) = 4.719$, $p < .05$) as the low AQ (fewer autistic traits) group showed a significant "anger superiority effect" while the high AQ (more autistic traits) group did not. Notably, AQ score did not influence sensitivity to walkers exhibiting any other emotions. Results from a separate control study with inverted walkers support the linkage between AQ and threat detection.

Conclusions: Psychophysical experiments examined the relationship between social skills and perceptual sensitivity to emotional human movement. The results indicate that typical adult observers with high AQ scores (more autistic traits) do not demonstrate heightened sensitivity to point-light displays of angry, and thus potentially threatening, human gaits. Conversely, typical observers with fewer autistic traits (low AQ) exhibit selectively enhanced visual sensitivity to such potential threat. These results (1) support the idea that autistic traits extend into the general population, (2) compliment and extend findings of impaired visual analysis of human motion in

individuals with autism, and (3) highlight the critical connection between social skills and visual sensitivity to negative emotions.

128.31 31 Ratings of Hypothetical Pain by Children and Adolescents with and without Autism Spectrum Disorders. N. F. Bandstra*, C. T. Chambers and S. A. Johnson, *Dalhousie University*

Background: Historically, there has been a belief that individuals with developmental disabilities/disorders (e.g., autism, Down's syndrome) do not experience pain. It is now generally accepted that this belief is false and that children with a variety of developmental disabilities are perfectly capable of experiencing pain. However, research continues to focus on the extent to which the experience and expression of pain is the same between children with developmental disabilities and their typically developing peers. Although parents of children with autism spectrum disorders (ASD) often describe their children's atypical responses to painful experiences, research specifically focused on how children with ASD experience and/or express pain is virtually missing from the pain literature. While one previous study (Nader, Oberlander, Chambers, & Craig, 2004) focused exclusively on pain in ASD, there were significant methodological limitations.

Objectives: The goal of this project is to compare the experience and expression of pain in high-functioning children and adolescents with ASD to typically developing children and adolescents.

Methods: To date, 28 participants (7-17 years-old), along with a parent, have completed the study. Fourteen of the participants were children/adolescents with an ASD, while the remaining participants were age-, gender-, and IQ-matched controls. Using two validated self-report pain assessment tools, participants were asked to rate the amount of pain they would expect to feel in a series of 17 hypothetical pain situations (e.g., falling down on pavement, receiving an immunization) depicted in gender neutral cartooned images. These ratings provide a measure of each child's *pain experience*. In order to gather a measure of *pain expression*, each child's parent was asked to rate the amount of pain they would expect their child to show in the same hypothetical pain situations depicted in the cartoons. A first-order theory of mind task was employed as a screening measure and participants were excluded if they did not pass this task.

Results: Children with ASD generally rated their pain in the hypothetical vignettes in a similar manner as did the children in the control group. When differences did emerge, they were always in the direction of ASD children rating the hypothetical pain situations as significantly more painful. The difference between each child and parent pair for each scenario was also calculated to create a discrepancy score. A group comparison of these discrepancy scores approached significance [$t\ (474) = -1.838$, $p = 0.07$] with parents in the ASD group rating their children as showing less pain than their children reported experiencing and parents in the control group rating their children as showing more pain than their children reported experiencing.

Conclusions: These preliminary findings suggest that children with an ASD report experiencing the same, if not greater, levels of pain as their non-ASD peers, but that they may be less likely to express this pain to their parents than their peers. These findings have important implications for how pain is assessed and treated in children with an ASD.

128.32 32 Food Selectivity and Sensory Issues in Children with Autism Spectrum Disorders. L. Bandini*[1], S. E. Anderson[2], C. Curtin[1], S. A. Cermak[3], E. W. Evans[4], R. Scampini[1], M. C. T. Maslin[1] and A. Must[5], (1)*University of Massachusetts Medical School*, (2)*The Ohio State University*, (3)*University of Southern California*, (4)*Children's Hospital Boston*, (5)*Tufts University School of Medicine*

Background: Although children with autism spectrum disorders (ASDs) are often reported to be selective eaters, an empirical definition of food selectivity (FS) has not been previously proposed.

Objectives: To develop an operational definition of FS, to compare FS among ADI-R confirmed children with ASDs to an age-matched sample of typically developing children, and to examine the relationship of FS to oral sensory sensitivity and sensory qualities of food.

Methods: We conceptualized FS as comprising 3 domains: food refusal, food repertoire, and high frequency single food intake (HFSFI). Food refusal and HFSFI were measured using a modified food frequency questionnaire (FFQ). Food repertoire was measured with the FFQ and a 3-day food diary. Child food refusal due to sensory characteristics of food was assessed with a diet history parent interview, and oral sensory

sensitivity was assessed with Dunn's Sensory Profile.

Results: Fifty-three children with ASDs (44 males/9 females) and 58 typically developing children (45 males/13 females) ages 3-11 (mean age 6.6 years) participated in the Children's Activity and Meal Patterns Study (CHAMPS). Thirty-two percent of children with ASDs also had intellectual disabilities. Compared to typically developing children, children with ASDs exhibited more food refusal and a narrower repertoire of foods eaten. Very few children in either group demonstrated HFSFI.

	ASDs	Typical
Food Refusal	Mean (SD)	Mean (SD)
Number of foods refused (out of 131)	45.2 (26.1)	21.9 (18.1) ***
Percentage of foods refused of those offered (%)	42 (25)	19 (16) ***
Number of vegetables refused (out of 26)	10.8 (6.4)	5.6 (5.2) ***
Percentage of vegetables refused of those offered (%)	63 (31)	33 (27) ***
Limited Food Repertoire		
Number of unique foods eaten during 3 days	22.7(6)	25.0 (6.0) **
Number of foods eaten at least once per week	29.8 (13.4)	40.2 (13.0) ***
High Frequency Single Food Intake		
Number (%) of children eating > 4.5 daily servings of a food	3 (5.6%)	1 (1.7%)

t-test: **p<0.01, *** p<0.0001

More parents of children with ASDs than of typically developing children reported food refusal based on consistency (77% vs. 36%), temperature (30% vs. 24%), shape (11.3% vs. 1.7%), and brand (15% vs. 1.7%) or when foods were mixed together (45% vs. 26%). Parents of children with ASDs and typically developing children reported similar rates of refusal based on the color of foods and whether foods were touching each other. As expected, food refusal correlated with oral sensitivity (r = -0.65, p<0.0001 in children with ASDs and r= -0.51, p<0.0001 in typical children).

Conclusions: Using our operational definition of FS, food refusal was significantly greater and food repertoire significantly narrower in children with ASDs than in typically developing children. Although HFSFI may be characteristic of some children's eating behavior, it does not appear to occur frequently among children with ASDs. Food refusal was related to sensory aspects of food and oral sensory sensitivity. Further research is needed to determine how FS impacts nutritional status and health of children with ASDs.

Supported by NICHD-R21HD48989

128.33 33 The Influence of Functional Play on the Development of Executive Functioning Skills and Aberrant Behaviors in Children with Autism. K. Stamper* and R. Bernier, *University of Washington*

Background: Reports of deficits in spontaneous and varied types of play are reported in autism and findings from several studies support impoverished play as evidenced by reduced complexity, flexibility, and frequency of play behaviors. Play provides opportunities for the mastery of skills in the cognitive, executive functioning, motor, and emotional domains (Ginsberg, 2007). The current study proposes that early play provides a rewarding activity in which executive functioning skills can be practiced and improved, and through improved executive functioning skills appropriate behaviors can be developed and enhanced.

Objectives: The objective of the current study was to use a longitudinal design to test the hypothesis that functional and imaginative play influences the development of executive functioning skills and aberrant behaviors in children with autism.

Methods: Participants included 58 children with autism spectrum disorder (aged 34-52 months; 47M, 11F) and 26 mental age-matched children with other developmental disorders (aged 33-57 months; 15M and 11F) participating in a larger longitudinal study of development. At time 1, functional play was assessed through a behavioral play assessment measure using dolls and objects and through ADOS codes of functional and imaginative play. Executive functioning (EF) abilities were measured 36 months later at Time 2 through an A not B task and a Spatial Reversal

task. At time 3, when the participants were approximately 9 years old, the Aberrant Behavior Checklist, a parent report measure, was administered to assess current autism symptomology. Relations between play skills, executive functioning skills, and autism symptoms were examined.

Results: The ASD group performed more poorly on measures of play than the DD group at all time points. After controlling for verbal IQ, correlations were found between play at Time 1, EF at Time 2, and stereotyped behaviors at Time 3 for children with ASD. For this group, functional play at Time 1 correlated with measures of EF at Time 2 on both an "A not B" task ($r = .262$, $p<.05$) and a Spatial Reversal task ($r = .453$, $p<.001$), as well as the Stereotyped Behaviors domain of the ABC at Time 3 ($r = -.352$, $p<.01$). However, no relationship between EF skills and behavior was observed. In contrast, for the DD group play at Time 1 did not correlate with EF at Time 2, but correlated with ABC domains of Irritability ($r = -.454$, $p<.05$), Hyperactivity ($r = -.613$, $p=.001$), and Inappropriate Speech ($r = -.427$, $p<.05$) at Time 3.

Conclusions: The current study shows that functional play skills may influence subsequent cognitive and behavioral development for children with autism, specifically EF abilities and stereotyped behaviors. However, the relationship between play and stereotyped behaviors is not mediated by executive functioning skills. Additionally, this developmental trajectory may be autism-specific, in that children with developmental disabilities matched on mental age showed no relationship between functional play and later EF skills or stereotyped behaviors. Instead, functional play was correlated with later development of other aberrant behaviors not specific to autism.

128.34 34 Sensory Processing Subtypes in Autism: Association with Adaptive Behavior and Autism Severity. A. E. Lane*[1], R. L. Young[2], A. E. Z. Baker[3] and M. T. Angley[3], (1)*The Ohio State University*, (2)*Flinders University*, (3)*University of South Australia*

Background: It is widely reported that children with autism frequently experience difficulties in sensory processing (Ashburner, Ziviani & Rodger, 2008; Baker, Lane, Angley & Young, 2008; Rogers & Ozonoff, 2005; Tomchek & Dunn, 2007). Direct reports from caregivers and adults with autism reveal a strong perception that negative behaviors associated with sensory processing difficulties are barriers to achieving competence in social participation and communication (Koenig and Kinnealey, 2008). Characteristic patterns of sensory processing in autism, however, are yet to be identified. It is also unclear how sensory processing difficulties contribute to the clinical presentation of the disorder.

Objectives: The aims of this study were twofold: 1) to describe patterns of sensory processing difficulties within a single diagnostic category of autism, and 2) to examine the relationship between sensory processing patterns in this group, adaptive behavior and autism severity.

Methods: Caregivers of children (n=54) with Autistic Disorder aged between 33-115 months were administered the Short Sensory Profile, the Vineland Adaptive Behaviour Scales and the Childhood Autism Rating Scale. Participants were recruited via an autism early intervention program and were either on the wait list, currently enrolled or had completed the program. Correlation, regression and model-based cluster analyses were used to examine the data.

Results: Model-based cluster analysis revealed three distinct sensory processing autism subtypes. These subtypes have been given the preliminary labels of: Sensory-Based Inattentive Seeking, Sensory Modulation with Movement Dysfunction and Sensory Modulation with Taste/Smell Dysfunction. Sensory subtypes were differentiated by the number of sensory domains affected and performance on taste/smell sensitivity and movement-related sensory behavior. Further, nearly all participants (92.6%) exhibited difficulties in auditory filtering. Sensory processing subtypes predicted communication competence and maladaptive behavior. Specifically, those participants with taste/smell dysfunction were noted to have the greatest communication impairment. Greater severity in sensory processing dysfunction was also highly predictive of maladaptive behaviors. Sensory subtypes were not strongly associated with autism severity.

Conclusions: This study found that children with Autistic Disorder exhibit three distinct sensory processing subtypes. These subtypes were found to be predictive of communication competence and maladaptive behaviors. Study findings suggest that consideration of the specific sensory

domains affected in autism rather than broad patterns of sensory under- or over-responsivity may guide more targeted and effective intervention strategies. Further, this study lays the foundation for the generation of more specific hypotheses regarding the mechanisms of sensory processing dysfunction in autism and supports the continued use of sensory-based interventions in the remediation of communication and behavioural difficulties in autism.

128.36 36 Development of Motor Coordination and Anticipatory Control in Children with Autism. D. Thorpe[1], G. T. Baranek*[1] and F. J. David[2], (1)*University of North Carolina at Chapel Hill*, (2)*University of Illinois at Chicago*

Background: Motor function has been rarely studied in persons with autism (ASD). Some studies provide insight into motor patterns in autism, but fail to address the development of these patterns, and rarely include comparisons with other developmental disabilities (DD), matched on mental age.

Objectives: Two experiments examine the motor coordination and anticipatory control during a grasping task in children with ASD to determine development and specificity of deficits.

Methods: Experiment 1 was quasi-experimental, contrasting ASD and typically developing (TD) groups (ages 8y2m -19y1m). Experiment 2 was quasi-experimental, contrasting autism, DD and TD groups., (ages 1y9m - 6y5m). Participants were recruited through an autism registry and collaborating projects/agencies. For both experiments, the dependent measures were onset latency between grip and load forces, grip force at the onset of load force, maximum grip force, and time to maximum grip force across three load categories (0.5N, 1.5N, and 3N). A pincer or three-jaw-chuck were used to grasp the experimental apparatus. Each subject performed 15 trials across 3 load categories (1N, 2N, and 4N). Data was processed and reduced using Datapac 2000. ANOVAs (group X load; group X load X age) were used to analyze the data..

Results: Experiment 1: Precision grip data were collected from 28 participants (ASD=14, TD =14), matched on chronological age and gender. Mean age was 11 years (range=8-19y). There was a significant main effect of group for grip to load force onset latency, $F(1, 78) = 9.855$, $p = 0.002$, and grip force at onset of load force, $F(1, 75) = 9.056$, $p = 0.004$. With respect to peak grip force, only the main effect for load was found to be significant, $F(1, 78) = 5.737$, $p = 0.005$. Similarly, for time to peak grip force only the main effect for load was significant $F(1, 78) = 4.213$, $p = 0.018$. Tukey's post hoc analysis revealed that for peak grip force and time to peak grip force 1 N load was significantly different from 4 N load, while the 2 N load was different from neither the 1 N nor the 4 N load categories. Experiment 2: Participants were 2-6 years (ASD=25; DD=13; TD=34 TD), matched on mental age. Analyses are in progress.

Conclusions: In Experiment 1, prolonged onset latencies indicated that during the initial phase of precision grip (i.e.prior to lift-off), participants with ASD exhibited serial control of grip and load forces as opposed to the parallel control demonstrated by their TD peers. After liftoff, participants with ASD exhibited a trend toward higher peak grip forces and longer time to peak grip forces compared to controls. The results of Experiment 2 will determine if abnormalities in precision grip are unique to autism as compared to DD and to what extent age is a mediating variable. Understanding the motor features of ASD will expand the diagnostic profile for persons with ASD and lead to more refined intervention strategies.

128.37 37 Is Emotion Recognition Impaired in High Functioning Individuals with ASDs?. R. A. Schriber*[1], J. L. Tracy[2], R. W. Robins[1] and M. Solomon[3], (1)*UC Davis Department of Psychology*, (2)*University of British Columbia*, (3)*MIND Institute, Imaging Research Center*

Background: Researchers have argued that individuals with autism spectrum disorders (ASDs) use an effortful "systematizing" process to recognize nonverbal facial emotion expressions, whereas typically developing (TD) individuals use a more holistic process. If this is the case, even high functioning individuals with ASDs, relative to TD individuals, should show slower, less efficient, and less accurate emotion recognition – a tendency that could help account for their social deficits. To date, research has been equivocal regarding whether high functioning individuals with ASDs have impaired recognition for emotion expression.

Objectives: The aim of the present research was to investigate the "systematizing" account of emotion recognition in ASD by testing whether children and adolescents with ASD show impaired recognition of basic-emotion expressions (anger,

disgust, fear, happiness, sadness, and surprise) and two more socially complex emotion expressions (contempt and pride). Specifically, we sought to investigate whether these individuals would exhibit a general deficit in recognition (i.e., lower accuracy and higher false-alarm rates relative to TD individuals), and whether they would recognize emotions through a more deliberate process (i.e., slower response times and below-chance recognition when forced to respond quickly). This was also the first study to examine whether individuals with ASDs can recognize the pride expression.
Methods: This study included 29 high functioning individuals with ASDs (3 female; *M* age=147 months) and 31 TD individuals (3 female; *M* age=147 months), all with Wechsler Full Scale IQ>75. Of the ASD sample, 11 were diagnosed with high functioning autism (HFA), 15 with Asperger's Disorder, and 2 with PDDNOS, according to criteria set by the DSM-IV-TR, the Autism Diagnostic Observation Schedule – Generic, and the Social Communication Questionnaire. Participants viewed blocks of photos of eight emotion expressions (anger, contempt, disgust, fear, happiness, pride, sadness, surprise). Each block had a different target emotion, and participants indicated whether each expression represented the target emotion for that block by pressing the "yes" and "no" keys on a keyboard. They were told to respond as fast as possible; the next expression appeared immediately after each response or after a maximum of 1500 ms.
Results: Children and adolescents with ASDs showed quick and accurate recognition for most emotions, including the socially complex emotion of pride. No differences emerged between ASD and TD groups on recognition rates, false alarm rates, and reaction times for any of the eight emotions. Furthermore, both groups tended to be more accurate when responding quickly, even though systematizing should promote a speed-accuracy trade-off for the ASD group.
Conclusions: These findings are not consistent with the systematizing account, and indicate that high functioning individuals with ASDs are not impaired in automatic emotion recognition.

128.38 38 A Novel Approach to Actigraphy in Children with Autism Spectrum Disorders. K. L. Surdyka*, K. Adkins, S. E. Goldman, D. Wofford and B. A. Malow, *Vanderbilt University*

Background: Sensory sensitivities are common in children with autism spectrum disorders (ASD) , Actigraphy, which uses activity and rest as measures of wake and sleep, has shown promise as a non-intrusive measure of sleep patterns in clinical trials to improve sleep in ASD. In contrast to polysomnography, actigraphy does not involve placing electrodes on the scalp, and data can be collected in the home setting for many days and nights. However, in our research of sleep and ASD, we encountered children who were not able to tolerate wrist actigraphy but were able to tolerate placement of the actigraph in the shoulder pocket of a shirt.
Objectives: We modified the placement of the actigraph to enclose it in the pocket of a cotton tee-shirt. The pocket measured 2"x2" and was attached to the outside of the shirt. We hypothesized that measurements of sleep latency (SL), total sleep time (TST), and movement and fragmentation index (MFI) would be comparable to wrist actigraphy.
Methods: To determine if sleep measurements were comparable between the two methods, we placed actigraphs in both locations (wrist and shoulder) on three children with ASD tolerant of wrist actigraphy All children wore the actigraphs (Mini Mitter, Respironics) on their shoulder and wrist for 1 week; children 1 and 2 wore loose-fitting shirts and child 3 wore a snug-fitting shirt. Wilcoxon signed ranks tests for non-parametric paired data were used to determine if the location of the watches yielded comparable results for SL, TST, and MFI.
Results: Wrist (W) and shoulder (S) measures of SL ($p = 1.0$); TST ($p = 0.25$), and MFI ($p = 0.25$) did not differ statistically. For all children, SL (in minutes) was very similar for the two placements, but closest in child 3 who wore the snug-fitting shirt. Values were: Child 1: SL (W) = 31.6, SL (S) = 30.9; Child 2: SL (W) = 12.9, SL (S) = 10.7; Child 3: SL (W) = 24.1, SL (S) = 24.6). For TST (minutes) and MFI, the two placements differed more than SL, but were relatively close in Child 3. Values were: Child 1: TST (W) = 421.4, TST (S) = 465.9, MFI (W) = 39.3, MFI (S) = 22.3; Child 2: TST (W) = 421.4, TST (S) = 465.9, MFI (W) = 39.3, MFI (S) = 22.3; Child 3: TST (W) = 415.1, TST (S) = 430.4, MFI (W) = 28.4, MFI (S) = 26.2.
Conclusions: Our preliminary results support the hypothesis that shoulder actigraphy may be a reasonable substitute for wrist actigraphy in children unable to tolerate the wrist placement, especially if the shirt used is snug-fitting. Studies comparing the two placements in larger numbers

of children will be necessary to confirm our results.

128.39 39 The Use of Social Observation in Predicting Variation in Outcome among Adolescents with High-Functioning Autism. C. Schwartz*[1], H. A. Henderson[2] and P. C. Mundy[3], (1)*Yale University*, (2)*University of Miami*, (3)*UC Davis*

Background: All individuals who are diagnosed with autism exhibit deficits in social and communication skills, and exhibit restricted repetitive behaviors. However, the adaptive life outcomes achieved by individuals with autism are extremely varied (Sigman & Ruskin, 1999). The modifier model of High-Functioning Autism (HFA; Mundy, Henderson, Inge, & Coman, 2007) suggests that studying non-syndrome specific constructs, which vary among all individuals regardless of diagnosis, provides insight into the processes by which some individuals with HFA succeed in leading independent lives while others require constant care and supervision.

Objectives: This study used a novel observational measure of social behavior as an outcome assessment, while also collecting information regarding temperament, symptoms, and social-emotional functioning, through observation and parent- and self-report measures, to examine individual variability in outcome.

Methods: A total of 58 participants (29 HFA, 29 Control) were seen as part of a larger longitudinal study examining motivation, self-monitoring, and family processes in higher functioning children with autism. Each group was composed of 5 females and 24 males. Each participant completed the self-report short form of the Early Adolescent Temperament Questionnaire- Revised (Ellis & Rothbart, 2001), which assesses temperament along 12 dimensions. The 12 dimensions are combined to form 4 overarching factors: Surgency (i.e., surgency/high intensity pleasure, shyness-reverse scored, fear-reverse scored), Effortful Control (i.e., attention, inhibitory control, activation control), Affiliativeness (i.e., affiliation, perceptual sensitivity, pleasure sensitivity), Negative Affectivity (i.e., frustration, depressive mood, aggression). In addition, each child in the HFA group was paired with a child in the control group and completed a dyadic social interaction. This interaction was composed of tasks such as an unstructured conversation in which participants were instructed to get to know one another, a teaching task in which each participants were given the opportunity to teach their peer how to complete a task, and a task in which participants were instructed to work together to make a list of the top ten movies ever made. From these tasks, measures of approach tendencies, social self-monitoring, and social skills were obtained. Parent-report of social-emotional functioning was also obtained on the Behavioral Assessment System for Children (Reynolds & Kamphaus, 2004).

Results: Results indicated that the HFA group self-reported higher levels of negative affect, $F(1, 52)=10.27$, $p<.01$, and lower levels of Surgency, $F(1, 52)=5.58$, $p=.022$, and were observed to exhibit higher levels of approach tendencies, $F(1, 56)=6.41$, $p=.014$, and lower levels of social skills, $F(1, 56)=16.14$, $p<.001$, compared with the control group. Across all participants, higher levels of Effortful Control, composed of self-report of effortful control and observed social self-monitoring, was predictive of more adaptive social skills, $F(5, 50)=6.57$, $p< .001$, and surprisingly, higher levels of observed approach behavior were predictive of higher levels of anxiety, $F(5, 52)=5.58$, $p< .001$.

Conclusions: These results will be discussed in relation to the variability in outcomes seen among individuals with autism. Strengths and limitations of the current observational paradigm and coding will be discussed as well as the importance of targeting self-regulatory skills (i.e., effortful control and social self-monitoring) in interventions for children and adolescents with autism.

128.40 40 Eye-Tracking Measures of Social Monitoring in Children with Autism. A. M. Krasno*, A. Klin and W. Jones, *Yale University School of Medicine*

Background: In previous research, we found that individuals with autism were significantly impaired in attributing social meaning to ambiguous visual information (the actions of animated geometric shapes). In another study, we measured visual scanning by individuals with autism while watching scenes of social interaction; their visual scanning showed evidence of altered visual salience and reduced social monitoring. In the present study, we used scenes from the classic children's film, The Red Balloon, to bring these two lines of research together. We defined a series of scenes in the film when a visual fixation to a particular location at a particular time would occur only as a consequence of a viewer's attribution of intentionality to the film's main characters, a boy

and his friend, the red balloon. Because the agency of the balloon is dynamic during the film—at times an ordinary balloon, at times an animate character—appropriate social monitoring is an indication of social attribution.

Objectives: To study social monitoring as a measure of implicit social attribution in individuals with autism.

Methods: 60 children with autism spectrum disorders (ASD) and 28 age- and IQ-matched typically-developing (TD) participants watched scenes from The Red Balloon while eye-tracking data were collected. Social monitoring was measured during scenes of interaction between the balloon and human characters. Three types of episodes were examined and defined as interactions between the following: 1) the boy and balloon before the balloon becomes animate, 2) the boy and balloon after the balloon becomes animate, and 3) the boy, the balloon after it becomes animate, and a third character. Social monitoring was defined as looking from the social actor (the balloon) to the social responder (the boy or third character) in order to gather implicit social information about how the social responder is reacting to the balloon's animacy.

Results: Analyses reveal significant differences in amount of social monitoring between groups. During episodes requiring social monitoring (type 2 and 3), the TD group looked to the social responder for a significantly higher percentage of time than the group with ASD. The TD group also looked back and forth between the social actor and social responder significantly more than the group with ASD, thus showing more monitoring of the actions and reactions of the characters. For these episodes, the more a participant with ASD differed from the TD participants' mean percent looking to the social responder, the greater the participant's autism severity (assessed by the social and communication subscales of the ADOS).

Conclusions: Our data show that individuals with ASD appear to be most impaired when the actions of others are dependent upon the balloon as an animate, intentional being. The present study offers a useful and non-verbal method of assessing social monitoring which could be used in evaluating outcome from social skills groups for individuals with ASD. In addition, it has the potential to reflect the individual's social profile pre- and post-social skills training.

128.41 41 Predictors of Social Communication Competence in a General Population of Children. D. H. Skuse*[1], W. Mandy[2] and J. Golding[3], (1)*Institute of Child Health*, (2)*University College London*, (3)*University of Bristol*

Background:

Population estimates of prevalence may underestimate autistic characteristics of lesser severity, for two main reasons. First, cases are usually ascertained from secondary screening, based on an initial selection of children with severe and obvious symptoms. Mild or moderate deficits in social and communicative competence may be missed, especially if associated with marked comorbidity such as conduct problems and ADHD. Second, methods of ascertainment are designed to maximise the distinction between valid cases of autism, defined according to conventional criteria, and to exclude conditions that do not quite reach diagnostic significance. In a recently reported study, the parent-report Social and Communication Disorders Checklist (SCDC) was administered to participants (n = 8,094) in the Avon Longitudinal Study of Parents and Children, when those children were approximately 92 months of age. We correlated impairment severity with independent clinical diagnoses of ASD, cognitive abilities, and teacher-rated maladaptive behavior. SCDC scores were continuously distributed in the general population; boys had mean scores 30% higher than girls. Social communicative deficits were associated with functional impairment at school, especially in the domains of hyperactivity and conduct disorders.

Objectives:

We aimed to ascertain predictors of social communication competence in a 24 month follow-up study of the original cohort,

Methods:

In this further study, the SCDC was administered again, to 6520 (80.6%) of the original sample, when they were approximately 116 months of age. Predictors (measured at 92 months) included: i) cognitive abilities; ii) teacher ratings of maladaptive behaviour on the Strengths and Difficulties questionnaire. Independent clinical identification of cases of ASD in the ALSPAC sample was obtained by 11 years of age.

Results:

Mean SCDC scores for children subsequently identified as having an autistic disorder (prevalence 0.69%) were almost identical at both time points (14.7/24). The strongest predictors of being in the highest decile of the distribution of SCDC scores at 116 months (independent of prior SCDC score) were: teacher rated hyperactivity, conduct disorder and peer problems at 92 months (all $p<0.001$), independent of verbal IQ and gender.

Conclusions:

We concluded from our earlier cross-sectional study that social and communicative deficits are of prognostic significance, in terms of behavioural adjustment at school, for both boys and girls. These new findings indicate the converse is also true. Children presenting with conduct problems at school in early adolescence may have undetected social communication difficulties.

128.42 42 Perception of Embarrassment in Adolescents with Asperger's Syndrome and Implications for Intervention. M. A. Winter-Messiers*, T. Oswald and L. Moses, *University of Oregon*

Background:

Embarrassment is the least researched of the self-conscious emotions among typically developing individuals (Hobson, 2006), and researchers have conducted even less research on embarrassment among individuals with Asperger's Syndrome (AS). Keltner and Buswell (1977) defined embarrassment as the outcome of violating rules of convention, threatening one's social identity within the interaction. Though studies are few, the anecdotal AS parent and clinic literature is replete with accounts of individuals with AS' negative verbal, emotional, and physical response to embarrassing situations.

Objectives:

We predicted that adolescents with AS would describe personal experiences of embarrassment that would not be perceived as embarrassing by TD controls, and would involve significantly more unusual and negative physical, emotional, and verbal responses than TD controls. We also predicted that although the AS group would be able to appropriately identify embarrassing vignettes (in contrast to their personal experiences), they would provide inappropriate justifications for their ratings, i.e., they can identify the experience but they cannot intuitively explain why something is embarrassing to them or others.

Methods:

40 male and female participants, aged 11-17, read 12 vignettes describing embarrassing situations, including physical, social, positive, and non-embarrassing situations. Participants were asked to rate the situations, and then asked to justify their ratings. We designed an instrument, "The Child Embarrassment Survey", used to interview participants about their definition of embarrassment, and what embarrassment looks like on the face, words, and actions of those who are embarrassed. We also asked participants to describe personal experiences with embarrassment at school, home, and in the community.

Results:

First, we found only slightly significant differences between the embarrassment vignette ratings of the AS and TD groups. In justifying their responses, however, the AS group showed a significantly poorer ability than the TD group to accurately explain why they had rated vignettes as embarrassing. Second, when asked to provide an embarrassing personal experience, we found that the AS group provided significantly fewer embarrassing experiences than the TD group. Raters reported that the events the AS group described would be perceived as non-embarrassing by most TD individuals. Third, the AS group described significantly more unusual and self-injurious behaviors in response to their personal experiences with embarrassment, e.g., picking at skin and drawing blood, hitting, and pulling hair. They further described a significantly higher rate of responses of anger, yelling, screaming, accusing others, and feeling stupid or worthless than the TD group. Finally, we found that the TD group spontaneously described amelioration strategies which they used to confront feelings of embarrassment, e.g., smiling.

Conclusions:

Adolescents with AS must be taught about the emotion of embarrassment, beyond the simple recognition of an embarrassing situation in a

photograph, and the amelioration strategies to navigate embarrassing situations. Further, we must research interventions that will support adolescents with AS in walking through their intense verbal, emotional, psychological, and physical responses. Dealing with embarrassment is a critical social skill and individuals with AS appear to find it painful. Research can lead us to interventions that may lessen these traumatizing responses.

128.43 43 Effects of a Clinic-Based Conversation Skills Group Training Program on Children with High Functioning Autism/Asperger Syndrome. A. Breit-Smith*[1], D. S. Murray[2] and C. A. Molloy[2], (1)*University of Cincinnati*, (2)*Cincinnati Children's Hospital Medical Center*

Background: One of the most powerful human abilities is the use of language in conversation as a means of relating to other humans. Children diagnosed with High Functioning Autism/Asperger Syndrome (HFA/AS), however, often have difficulty conversing. As a result, speech-language pathologists have developed and implemented clinic-based social skills groups. These training programs are designed to improve the conversation skills of children with HFA/AS. Although clinicians intuitively perceive the benefits of social skills group training programs, there is inconclusive evidence to support clinical practice.

Objectives: The objective of this study was to explore the effects of teaching conversation skills, namely appropriate initiations and responses, to children diagnosed with HFA/AS in an outpatient clinic-based group setting. This study included three research questions: 1) Is there a difference between pre and post clinic observation of participants' initiations and responses during conversation after they participate in an outpatient clinic-based intervention group training program? 2) Is there a difference between pre and post clinic observation in the appropriateness of initiations and responses after participating in an outpatient clinic-based intervention group training program? 3) Is there a difference between pre and post clinic observation in the proportion of initiations and responses participants direct towards peers as compared to adults during conversation after completion of an outpatient clinic-based intervention group training program?

Methods: Seven boys between the ages of 8 and 10 years old participated in this study. The boys attended a 6 week conversation skills group intervention program that met one time per week for 90 minutes. This study utilized an observational design. Prior to, immediately after and 6 weeks following the intervention, data regarding the children's initiations, responses, appropriateness and partner (peer/adult) during conversation was collected in-clinic, as well as at participants' schools. Descriptive measures for this study included frequency counts, ratios, means and difference scores for each child.

Results: Results from this study revealed an increase in the frequency of responses used in-clinic, as well as an increase in participants' use of initiations at school at post observation. Little to no maintenance of the increase in initiations, noted at post observation, was observed at the 6 week follow-up observation. No major trends, only slight increases and decreases, were noted both in-clinic and at school regarding appropriateness and to whom participants directed their initiations and responses to (peer/adult) during conversation.

Conclusions: The descriptive information acquired from this study suggests that for children with HFA/AS, small group direct instruction of initiations and responses during conversation in-clinic may be useful for increasing those behaviors, but only in the short-term. In addition, this study demonstrates the feasibility of recording and gathering observational data on elements of conversation in a natural environment such as school. Finally, the preliminary data from this study provides a target effect size and estimate of variability for designing more definitive intervention studies.

128.44 44 Social Stories to Improve Social Skills in Children with Autism Spectrum Disorder: a Systematic Review. B. G. Clark* and M. Karkhaneh, *University of Alberta*

Background: Over the past 20 years a variety of treatment approaches have been developed for and applied to children with Autism Spectrum Disorders (ASD) to remediate the core deficits. Since the early 1990s, Social Stories have been suggested to positively affect the pro-social development of children with ASD and much effort has been made to justify their expanded use.

Objectives: Our objective was to conduct a systematic review of the literature on the efficacy and effectiveness of Social Stories in the treatment of autistic children.

Methods: Using pre-defined, rigorous methods, two reviewers independently screened articles for inclusion, applied study eligibility criteria, extracted data, and assessed methodological quality. Results: A qualitative analysis was conducted on six eligible controlled studies.

Table 1: Overview of Study Objectives, Design, and Sample Characteristics

Andrews 2004	To increase game playing skills, story comprehension, and social skills comprehension	RCT (parallel)	20 (NR)	8-12 (10)	Severity not reported; children were verbal and could read and understand written words at or above first grade level	DSM-IV-TR, ADOS-G (NR)	CCT (parallel)	10 (50%)	4-8 (6)	Child comm (expr need verba verba augm manu comm board modi langu
Bader 2006	"To increase emotion recognition and labeling skills"	RCT (crossover)	20 (NR)	6-13 (9)	Severity not reported; children were verbal and could read and understand written words at or above kindergarten grade level	DSM-IV-TR, ADOS (NR)				
Feinberg 2001	To increase four specific social skills during game playing	RCT (parallel)	34 (74%)	8-13 (10)	Moderately severe symptoms; children had at least phrase speech	DSM-IV, ADOS-G, ADI-R, CARS (NR)				
Quirmbach 2006	1) To increase game playing skills and story comprehension; 2) to compare different story formats; 3) to assess children's ability to	RCT (parallel)	45 (93%)	7-14 (??)	Children could read at or above first grade level; 42/45 children diagnosed with autism and 3 with ASD	DSM-IV-TR, ADOS (NR)				
Ricciardelli 2006	To improve five specific pro-social behaviors	CCT (parallel)	6 (100%)	10-13 (11)	Cogn avera avera skills					
Romano 2002	To reduce inappropriate communication, aggressive behaviour, and inappropriate socialization behaviours	CCT (parallel)	10 (50%)	4-8 (6)	Child comm (expr need verba verba augm manu comm board modi langu					

RCT=randomized controlled trial; CCT=controlled clinical t

Conclusions: Of the six unpublished controlled trials (four RCT, two CCT) evaluating the effect of Social Stories on ASD patients, five (four RCT and one CCT) concluded that social stories are effective in terms of decreasing aggressive behavior, improving communication and socialization skills, teaching social skills, increasing game playing skills, enhancing comprehension and generalizing social comprehension, and increasing facial emotion learning and labeling. One study also demonstrated that both standard and directive story formats can be equally effective in eliciting game play skills.

128.45 45 Social Orienting Impairment in Autism: Relations among Looking Length, Disengagement Latency, and Symptom Severity. L. E. Bahrick*, J. T. Todd, M. Vaillant, Molina, B. M. Sorondo and I. Castellanos, *Florida International University*

Background: Children with autism spectrum disorders (ASD) show impairments in social orienting, with slower times to orient and less looking to social versus nonsocial events (Dawson et al., 2005). Our prior study (Newell et al., 2007) revealed social orienting impairments in ASD, with reduced looking to social events, particularly affectively positive infant directed speech, but comparable looking to nonsocial events relative to

TD children. Affectively positive infant directed speech exaggerates intersensory redundancy (rhythm, tempo, and intensity changes common to audible and visible stimulation). Intersensory redundancy is highly salient and underlies the typical development of social orienting (Bahrick, 2008).

Objectives: To more precisely characterize social orienting impairments in autism and their relation to symptom severity, we explored in finer detail the nature of attention to social versus nonsocial events in ASD and TD children from our prior study. We expected social orienting impairments to be demonstrated in children with ASD by more disengagement and shorter looks to social events, particularly affectively positive social events and that greater social orienting impairments would be related to greater symptom severity among children with ASD.

Methods: Eleven children with ASD (M=3.6 yrs) and 11 TD children (M=2.1 yrs) matched on functional age (using the ABAS) were tested in the Behavioral Attention Assessment Protocol (Newell et al., 2007). In this procedure, children receive trials of a central stimulus (3s) followed by two side-by-side peripheral events (10s) along with the soundtrack to one event. Blocks of trials depicted nonsocial, social neutral, and social positive events. The proportion of available looking time, number of disengagements per minute, and average length of look to the peripheral events were calculated.

Results: ANOVAs indicated that children with ASD showed more disengagements per minute and shorter looks than TD children (*p*s< .005), particularly for social, but not nonsocial events. Children with ASD showed reduced overall looking to social positive events compared with TD children (p =.02), but comparable looking times overall.

Analyses of symptom severity (measured by the Social Communication Questionnaire) revealed a significant negative correlation between severity and looking time to social positive events (r =-.74, p <.01), with less looking associated with more symptoms. Children with ASD with more symptoms (according to a median split) showed shorter looks (p=.02) and more disengagements, particularly for social positive events (p=.007), and less overall looking to social positive events than children with ASD with fewer symptoms (*p*s<*.01*). Furthermore, children with more symptoms differed from TD children on all measures (*p*s<.01), whereas those with fewer symptoms did not.

Conclusions: Results demonstrate that children with ASD show social orienting impairments with less looking time, more disengagements, and shorter looks to social events, particularly affectively positive speech, than TD children. Moreover, greater symptom severity is associated with greater impairment. Affectively positive events provide high intersensory redundancy, an important basis for social orienting in typical development. Measures of disengagement and look length reflect important individual differences in attention underlying social orienting. These findings suggest a link between symptom severity and intersensory processing disturbance in autism.

128.46 46 Critical Self-Referent Attributions Potentiate Social Skills Intervention Response in Adolescents with Asperger Syndrome & High-Functioning Autism. M. D. Lerner*[1], J. R. Spies[1], B. L. Jordan[2] and A. Y. Mikami[1], (1)*University of Virginia*, (2)*McLean Hospital*

Background: A need exists for empirically-validated interventions addressing social skills in adolescents with autism spectrum disorder (ASD) and for a greater understanding of mechanisms of change in interventions (White, Keonig, Scahill, 2007; Kazdin, 2008). Critical self-referent attributions (CSA)—social cognitions representing the tendency to derive pejorative self-evaluations from ambiguous peer cues—have been shown to be associated with actual peer experiences and are thought to be linked to maladaptive social behaviors and depressive symptoms in typical child populations (Prinstein, Cheah, Guyer, 2005), but to our knowledge have never been assessed in ASD populations. Given the high rates of these symptoms in adolescents with asperger syndrome (AS) and high-functioning ASD (HFA) (Williamson, Craig, Slinger, 2008), we expect CSA to be relevant in this population. Given that CSA entails a heightened sensitivity to social failure, we hypothesize that it may facilitate receptiveness to interventions designed to address such failure, thereby potentiating social skills intervention effects.

Objectives:

1. To ascertain whether participation in the six-week Socio-dramatic Affective-Relational

Intervention (SDARI; Lerner, Mikami, & Levine, *under review*; Lerner & Levine, 2007) is effective in improving parent-reported social skills as compared to a matched comparison group.

2. To determine if baseline CSA predicted response within this intervention.

Methods: This study included 35 participants with AS and HFA divided into a SDARI intervention group (n=27. 22 male, 5 female; mean age=13.1) and an age, sex, and diagnosis-matched comparison group (n=8, 6 male, 2 female; mean age=14). Multilevel modeling was used to model change across both the SDARI and comparison conditions. The parent-report Social Responsiveness Scale (SRS; Constantino, 2002), thought to be relevant to ASD and sensitive to change (White et al., 2007), was used to measure treatment response at 3 week intervals beginning six weeks prior to intervention to 6 weeks post-intervention. The Hostile Attribution Questionnaire (adapted from Prinstein, et al., 2005) was used to measure CSA, and was administered during the second week of SDARI.

Results: When comparing the SDARI and comparison groups on SRS across time, slope was significantly predicted by both time (β=-0.402, p=.002) and intervention status (β=-0.496, p=.017), indicating improvement over time in both groups, but significantly greater improvement in the SDARI group. When entered as a predictor at the random level, CSA significantly predicted slope (β=-0.743, p<.05), indicating greater intervention responsiveness among those with higher CSA at baseline.

Conclusions: Results support the hypothesis that SRS ratings of SDARI participants improve over time relative to comparison condition participants, and that CSA is a significant predictor of these effects. Those with higher CSA seem to benefit more from SDARI than those with lower CSA, indicating either that SDARI may be optimally effective for ASD individuals who are highly self-critical or that such individuals may be more receptive to social skills interventions in general. Further research should assess both the specific efficacy of SDARI for ASD populations and the role that social cognitive factors such as CSA play for this population in terms of both taxonomy and intervention.

128.47 47 Improving Social Skills in Adolescents with Autism Spectrum Disorders: The Adaptation of the UCLA PEERS Program into a School-Based Teacher-Assisted Intervention.

R. W. Ellingsen*[1], E. Laugeson[2], J. Sanderson[2], J. Lee[1], A. Lenvin[1], J. McNamara[1] and F. Frankel[2], (1)*University of California, Los Angeles*, (2)*UCLA Semel Institute for Neuroscience & Human Behavior*

Background: Teens with Autism Spectrum Disorders (ASD) typically display deficits in social skills, committing infractions of rules of social etiquette that often lead to negative reputations, peer rejection, social isolation, withdrawal, and loneliness. Although typically-developing teens often learn basic social rules through observation of peer behavior and/or specific instruction from parents, adolescents with ASD often require further instruction. By teaching appropriate social skills and improving the quality of friendships for adolescents with ASD, we may promote positive social skills which could impact current and long-term adjustment. Consequently, social skills training has become a popular method for helping adolescents with ASD more effectively adapt to their social environment. Yet, very few social skills intervention studies have taken place in the classroom, arguably one of the most naturalistic social settings of all. Previous studies have also typically failed to include teachers as interventionists, perhaps underutilizing the powerful impact of school-based treatment.

Objectives: This study, which is currently under investigation, seeks to examine the change in social functioning among teens with ASD following the implementation of a 12-week school-based teacher-assisted social skills intervention compared to teens in an active treatment control group.

Methods: Utilizing adapted treatment protocol from the UCLA PEERS Program, a parent-assisted evidence-based social skills intervention for teens with ASD, sixty participants will be recruited across six middle school and high school classrooms at The Help Group's Village Glen School, a nonpublic school serving adolescents with ASD. Each of the six classrooms, comprised of approximately 10 students each, will be randomly assigned to one of two conditions: Treatment group (n = 30) or Active Treatment Control group (n = 30). Participants will receive daily social skills instruction for 30 minutes a day in both conditions. Participants in the Active Treatment Control group will receive the typical

Village Glen school-based social skills scope and sequence. Participants in the Treatment group will receive the 12-week teacher-assisted PEERS intervention. Teachers assigned to the treatment condition will be trained and supervised in all aspects of the intervention. Key elements of the intervention will be taught didactically through instruction of simple rules of social etiquette. Newly learned skills will be rehearsed in the classroom, while teens receive performance feedback from their teachers during behavioral rehearsal exercises. Teens will also be required to complete weekly socialization homework assignments, which will help generalize the training outside of the classroom. Parents will receive weekly handouts to provide instruction about how to help their teen make and keep friends.

Results: Forthcoming preliminary findings are anticipated to reveal that teens in the PEERS teacher-assisted social skills condition will exhibit significantly greater improvement in their social functioning and friendship skills compared to teens in the active treatment control condition, according to self-reports, teacher-reports, and parent-reports.

Conclusions: Findings are anticipated to suggest that the use of the PEERS teacher-assisted social skills intervention is effective in improving the social competence and friendship skills of teens with ASD.

128.48 48 Modification of An Emotion-Based Social Skills Training Program for Children with Autism and Mild Intellectual Disability. B. Ratcliffe*[1], V. J. Grahame[2] and M. G. Wong[3], (1)*Children's Hospital at Westmead; Charles Sturt University*, (2)*Fleming Nuffield Unit*, (3)*Children's Hospital at Westmead*

Background: Autism is a developmental disability characterised by qualitative impairment in social skills, communication skills and restricted and repetitive behaviour. Approximately 70% of children with Autism will have a Learning Disability. Research suggests that children with Autism are at significantly increased risk of developing mental health problems during childhood and later in life. Children with Autism and Learning Disability, (defined as IQ<70 on an individually administered test of intelligence and associated delays in adaptive behaviour), are more vulnerable as they have additional learning problems alongside these social and emotional deficits. These additional deficits may increase the risk of psychopathology. It is therefore hypothesised that the development of an intervention to increase social and emotional skills in these children will reduce risk of mental health problems and improve psychological well-being.

Emotion-based Social Skills Training is a novel intervention that was originally developed to help children with Asperger's Syndrome understand their own and others' emotions, as well as regulate their emotions. This training uses developmental models of social and emotional development, emotional competence, and emotional intelligence. It has been shown to be effective for children with Asperger's Syndrome in two pilot studies.

The current study has modified the Emotion-based Social Skills Training by a team comprising of clinical psychologists and speech language pathologist to address the specific learning needs of children with Autism and Learning Disability. Program modifications include the use of video modelling, video social stories, and augmentative and alternative communication strategies to support children's language ability.

Objectives: The pilot study was designed to first modify the Emotion-based Social Skills Training program for children with Autism and Learning Disability, and then secondly to compare and evaluate the modified Emotion-based Social Skills Training with the original program.
Methods: The modified program was piloted on 5 children (aged 8-12 years) with a diagnosis of Autism (assessed using the Autism Diagnostic Interview-Revised and Autism Diagnostic Observation Schedule) and a Learning Disability (assessed using the WISC-IV and ABAS-II).
The pilot group was divided into three Modules: Identifying emotions; Understanding others' emotion and Managing emotions. Parents were asked to attend concurrent sessions to develop their skills as emotion coaches for their child. This was designed to increase likelihood of skill practice at home, and to promote generalisation across settings. The pilot study was evaluated using pre and post-treatment assessment (measures included parent and teacher reports of social skills, emotional well-being, and behaviour), parent and child qualitative questionnaires as indicators of program acceptability and feasibility, and independent clinician-rated home observations of parent-child

interactions before and after the training. Results: The results will be presented in terms of their effectiveness in improving children's social and emotional well-being, reducing anxiety and depression scores and impact on parental mental health and confidence.

Conclusions: The effectiveness of a modified Emotion-based Social Skills Training for children with Autism and Learning Disability will be compared with results from the original program.

128.49 49 Cognitive Profiles and Social Presentation: An Early Analysis of Data from the Autism Center of Excellence and Simons Simplex Collection Studies at UIC. P. Cali*, J. Klaver, R. Loftin, M. Huerta, C. W. Brune and E. H. Cook, *University of Illinois at Chicago*

Background: Limited efforts have been made to clearly define the relationship between cognitive ability and social presentation in individuals with autism spectrum disorders (ASDs), although both vary widely within this population. Intelligence quotients (IQs) for individuals with ASDs range from the immeasurably low to immeasurably high. Unusual splits in cognitive ability are common. For example, relative, and often normative, strengths in verbal ability occur alongside visual-spatial processing deficits with high frequency in individuals with higher functioning autism and Asperger Disorder (Williams, Goldstein, Kojkowski, & Minshew, 2008). However, strength in visual processing and relative deficit in verbal processing are commonly observed in Autistic Disorder (Happé, 1994). These "splits" may have some relationship to social presentation. For example, Joseph and colleagues found an inverse relationship between verbal IQ scores and social-communication symptoms of ASD among participants whose verbal IQ was significantly higher than nonverbal (2002). The reverse profile was observed among children whose nonverbal IQ was greater than verbal. Other studies have suggested that higher verbal IQ does not readily translate to better adaptive social functioning (e.g., Klin et al., 2007).

Objectives: Broadly, this study will explore the relationship between cognitive profiles and social phenotype in individuals with ASDs. Specifically, the authors will investigate whether the suspected inverse relationship between IQ and social engagement and interest is present. Further, for those individuals with significant VIQ/NVIQ splits (i.e., a difference of more than 1.5 standard deviations), the relationship between cognitive functioning and social engagement and interest will be examined to determine whether there are differences in the VIQ>PIQ and PIQ>VIQ groups.

Methods: Participants will include approximately 120 individuals, ages 3-28years, participating in genetic studies of autism with a clinical diagnosis of an ASD based on the Autism Diagnostic Interview-Revised (ADI-R), Autism Diagnostic Observation Schedule (ADOS), and DSM-IV. Measures of cognitive functioning were chosen based on the participants' age and language level, and included the DAS-II, WISC-IV, and WASI. Dimensions of social functioning will be measured by subdomains on the Autism Diagnostic Interview-Revised (ADI), the Autism Diagnostic Observation Schedule (ADOS), and the Social Responsiveness Scale (SRS). Participants' social presentation will be compared with verbal, non-verbal, and overall IQ scores in order to better understand the relationship between social presentation and cognitive functioning. The variance of IQ scores within groups will also be compared. Age and sex will be included as covariates in the analyses. The distribution of social presentation by cognitive functioning and by VIQ differing more than 1.5 standard deviations from NVIQ will be assessed.

Results: Results of the data analysis described above will be presented.

Conclusions: These results will suggest whether expectations about social phenotypes and cognitive profiles are supported in this relatively diverse sample of individuals with ASD.

128.51 51 Functional Analysis of Social Behavior in Children with Autism. M. A. Conroy*, *Virginia Commonwealth University*

Background: The display of early social communicative behavior is considered a pivotal skill for young children with autism spectrum disorders (ASD) (Koegel et al., 1999). A number of treatments have been prescribed (e.g., adult and peer mediated, antecedent interventions) to remediate early social-communicative skill deficits; however, many of these treatments suffer from a lack of empirical evidence substantiating sustained positive effects (Rogers, 2000; McConnell, 2002) and do not include an analysis of the environmental contributors that may facilitate or inhibit skill development (Conroy et al., 2007). Functional analysis is an effective assessment tool used to evaluate the environmental contributors to aberrant behavior

displayed by children with ASD (Carr et al., 1999; Iwata et al., 1982/1994). Although frequently used to design treatments for individuals with ASD who demonstrate aberrant behavior, functional analysis has not been extensively applied to other forms of behavior, such as social communicative skills. Since deficits in social communicative behavior is considered a key feature of ASD and is an important skill to acquire, the purpose of this study was to investigate the use of functional analysis methodology to analyze the maintaining consequences of social communicative behavior in young children with ASD. Objectives: Aim 1: To apply the use of a functional analysis (FA) protocol to determine the functions of prosocial behaviors in children with Autism Spectrum Disorders (ASD). Aim 2: To determine the extent to which functions of prosocial behaviors systematically differ across social subtypes of children with ASD. Methods: Participants were 30 young children, ages 3 – 9 years, who have been diagnosed with ASD and demonstrated deficits in social communicative skills. Procedures for addressing Aim 1 included the development of a functional analysis protocol to identify functions of social communicative behaviors. A within subject alternating treatments design was used to analyze three potential functions of social communicative behavior (e.g., attention, tangible, escape) in comparison to control conditions. Direct observation of social behaviors (rpm) was used to measure the relative differences across conditions. Interobserver agreement was obtained on with an average of 92%. Procedures for addressing Aim 2 included the Wing & Attwood (1987) social subtype classification system. A 3 x 3 repeated measures ANCOVA (analysis of covariance) was employed to determine statistical differences in function and social subtypes of autism. The Leiter-R and the CELF(Preschool or 3) standard total language scores were used to control for variance due to I.Q. and communication differences, respectively. Results: The findings indicate the utility of using functional analysis methodology to identify functions of social communicative responses in children with ASD. Functional analysis data indicated that the majority of the children demonstrated social communicative behavior to obtain a preferred tangible item. However, obtaining attention and escaping social attention were also displayed. No significant findings were indicated based on social subtypes of ASD. However, findings indicated that IQ and language levels were related to function. Conclusions: Data will be discussed in terms of implications for treatment.

128.52 52 Participation of Children with ASD in Social, Recreational, and Leisure Activities. A. Solish*[1], A. Perry[2] and P. Minnes[3], (1)*York University*, (2)*Thistletown Regional Centre*, (3)*Queen's University*

Background: Participation in activities can afford children opportunities for social interaction, social skill and friendship development, as well as improved mental and physical health and self-worth (e.g., Buttimer & Tierney, 2005; Cowart, Saylor, Dingle, & Mainor, 2004; King et al., 2003). However, children with disabilities engage in fewer activities, and when they do participate often do so primarily with adults (Cowart et al., 2004; Modell, Rider, & Menchetti, 1997; Orsmond, Krauss & Seltzer, 2004; Sloper, Turner, Knussen, & Cunninghan, 1990).

Objectives: The current study examined the activity participation of children with autism or an autism spectrum disorder (ASD), and compared this participation to that of typically developing children (TD) (children who did not have any known diagnoses) and children with a diagnosis of an intellectual disability (ID).

Methods: Participants were parents of 185 children (114 male) divided into three groups: children with an ASD with or without a comorbid ID (n = 65), TD children (n = 90), or children with ID without ASD (n = 30). Parents completed a questionnaire designed for this research reporting about their child's participation in social, recreational, and leisure activities. Social activities referred to informal activities with peers (e.g., playing at friends' houses), recreational activities referred to more formally organized and structured activities (e.g., playing on a hockey team/taking music lessons), and leisure activities referred to more passive activities (e.g., playing on the computer). Parents were also asked "with whom" each activity was completed (i.e., with peers, parents or other adults).

Results: The TD children participated in significantly more social and recreational activities than the children with either ASD or ID. Children in all three groups participated in a similar number of leisure activities. The TD children participated in a significantly greater percentage of their social and recreational activities (but not leisure activities) with peers. Children with either

ASD or ID participated in proportionately more social activities with parents and with other adults. The TD children had significantly more "mutual friends" and "best friends". Comparing the ASD and ID groups specifically, the children with ASD participated in substantially more leisure activities with adults than the children with ID. Furthermore, the children with ASD participated in significantly fewer recreational activities with peers than the children with ID. Finally, the children with ID had more friends and were more likely to have a best friend than were the children with ASD.

Conclusions: This pattern of results was not surprising given the social impairments inherent in a diagnosis of ASD. However, these findings also suggest that children with ASD are at an increased disadvantage when interacting with peers and engaging in activities independent of adults. When conducting research on activity participation, combining children with different diagnoses into one group and/or amalgamating social, recreational, and leisure activities into general activity participation may obscure important differences. Future research in this area should continue to take into account not only whether children are engaging in activities but explore more precisely "with whom" these activities are occurring.

128.53 53 Empathy in High-Functioning Autism. A. Newbigin*[1] and C. Dissanayake[2], (1)*Olga Tennison Autism Research Centre, La Trobe University*, (2)*La Trobe University*

Background: Hobson, Harris, García-Pérez and Hobson (in press) reported that mixed ability children with autism looked less at, and showed less concern for, someone expected to experience a negative feeling. Sigman, Kasari, Kwon and Yirmiya (1992) found that children with autism were less responsive to expressed distress, fear and discomfort, and Dissanayake, Sigman and Kasari (1996) found a similarly lowered level of responsiveness to expressed distress and anger among children with high-functioning autism (HFA). Children with autism have also been found to show fewer prosocial behaviours compared to matched controls (Travis, Sigman & Ruskin, 2001).

Objectives: The aim in the study reported here was to investigate how children with HFA respond to 1. expressed distress and 2. to someone expected to experience distress. The role of self-understanding in understanding and responding to others was also investigated.

Methods: Twelve with HFA and twelve typically developing (TD) children were tested. To test responsiveness to someone expected to experience distress, each child completed a drawing task with two experimenters (E1 and E2) in which the child, E1 and E2 each drew a picture. At the end of this task, E1 tore up the drawing done by E2. Groups were compared on the degree of concern expressed for E2. To test responsiveness to expressed distress, E1 pretended to misplace her watch and feigned distress before searching for it. Groups were compared for degree of concern and prosocial behaviours. In addition, children were asked to describe and explain their responses to each scenario while viewing video of these tasks, to gain their own perspective of their social understanding and responsiveness.

Results: The results thus far are congruent with the pattern of results obtained in previous research, as children with HFA showed less concern towards others who express distress and who might be expected to experience distress. Scores on each of these tasks will be interpreted in light of children's self-understanding measured using the Self-Perception Profile for Children (Harter, 1985), understanding of themselves in relation to important others and children's own descriptions and explanations of their responses to these tasks (data not yet available).

Conclusions: Children with HFA show a lowered level of responsiveness to expressed emotion and to someone expected to experience distress even though they appear to be aware of the situations which elicit negative emotions. Children's own descriptions and explanations of their responses to these tasks provide further insight into their responses than have heretofore been described.

128.54 54 A Randomized Control Trial of Reciprocal Imitation Training in Young Children with Autism. B. Ingersoll* and N. Bonter, *Michigan State University*

Background: Children with autism exhibit significant deficits in imitation skills. Reciprocal Imitation Training (RIT), a naturalistic imitation intervention, was developed to teach young children with autism to imitate during play. Previous research employing multiple-baseline designs has shown this approach to be effective for teaching object (Ingersoll & Schreibman,

2006; Ingersoll & Gergans, 2007) and gesture imitation (Ingersoll, Lewis, & Kroman, 2007) in young children with autism.

Objectives: The goal of this study was to examine the efficacy of RIT in a larger sample of children using a randomized control trial and standardized assessments.

Methods: Twenty-one children with autism between the ages of 2 and 4 were randomly assigned to a treatment (11) or control (10) group. Children in the treatment group received 3 hours per week of RIT targeting object and gesture imitation for 10 weeks. All participants were administered standardized assessments of imitation skills at pre- and posttreatment, and at a 2 month follow-up.

Results: Preliminary results suggest that children in the treatment group made greater gains in imitation skills than the control group.

Conclusions: RIT is an effective approach for teaching imitation skills to young children with autism.

128.55 55 CBT Social Skills Intervention for School Aged Boys with ASD. C. Koning*[1], W. Mitchell[2], J. Magill-Evans[1] and J. Volden[1], (1)*University of Alberta*, (2)*Glenrose Rehabilitation Hospital*

Background: School-aged children with Autism Spectrum Disorder (ASD) experience significant difficulty with peer interaction, an important occupation of childhood. Unresolved social skills difficulties lead to continued dysfunction in relationships which influence long term success. Research into the most effective strategies has increased but several questions remain. One approach that appears to help school-aged children is Cognitive Behavior Therapy (CBT) which focuses on changing how a person thinks about specific social situations as well as how they behave (Bauminger, 2006 a, b).

Objectives: This study investigated whether group social skills intervention based on CBT significantly improved the social skills of school-aged boys with ASD.

Methods: Ten boys aged 10-12 who met criteria for ASD based on expert clinical opinion using DSM IV criteria and confirmed by administering the ADOS (Lord, Rutter, Dilavore & Risi, 1999) were participants. Participants also met inclusion criteria of full scale IQ and receptive language greater than 80. They were randomly assigned to treatment versus waitlist control group. Intervention was delivered in fifteen weekly 1.5 hour sessions, first to the treatment group and then to the waitlist control group, using a curriculum (Baker, 2003; Garcia-Winner, 2005) based on the principles of CBT. Three of the fifteen sessions were intended to focus entirely on practicing skills in fun activities without specific social skills instruction. The other sessions included topics such as learning to read nonverbal cues, understanding another person's perspective, starting and maintaining conversations, dealing with difficult social situations and general social problem-solving. Group size varied from four to six participants. Pre and post intervention scores were collected in the domains of peer interaction, social perception, pragmatic language, social responsiveness, general adaptive behavior in the area of socialization and general social knowledge.

Results: This poster describes the intervention program and specific changes in selected social skills and social knowledge for participants in the CBT group intervention program using repeated measures t-tests. Comparison of the intervention and waitlist control group will also be reported. Responsiveness of measurement tools will be presented.

Conclusions: CBT holds promise for high functioning children with ASD. This pilot research provides direction for therapists considering using group-based CBT to improve social interactions.

128.56 56 Concomitant Gains in Joint Attention Via Naturalistic Communication Intervention. A. B. Cunningham*[1], J. Suhrheinrich[1], L. Schreibman[1], A. Stahmer[2], R. L. Koegel[3] and L. K. Koegel[3], (1)*University of California, San Diego*, (2)*Rady Children's Hospital*, (3)*University of California, Santa Barbara*

Background: The Picture Exchange Communication System (PECS) and Pivotal Response Training (PRT) are empirically-based programs for teaching communication skills to children with autism. As these naturalistic interventions teach communication skills, research has primarily addressed gains in these areas. The treatment literature emphasizes the importance of targeting core autism deficits (e.g., joint attention). Little research has evaluated concomitant gains in these behaviors as a result of naturalistic verbal and augmentative communication interventions.

Objectives: To assess collateral gains in joint attention skills and other social communicative behaviors not directly targeted by the interventions.
Methods: Thirty-five children with autism (age 2-4), with 10 or fewer functional words, were randomly assigned to PRT (n=17) or PECS (n=18). Children were matched on pre-treatment age, word use, and developmental level. Children received 258 hours of intervention across 23 weeks. Participants were assessed using the Early Social Communication Scale (ESCS) at pre- and post-treatment.
Results: Participants showed improvements in behaviors targeted through PECS and PRT, such as verbal language to request. Participants also demonstrated concomitant gains in rate of high-level joint attention initiations, and frequency of responding to the assessor's social invitations, bids for joint attention, and receptive commands (i.e. "Give it to me").
Conclusions: While as expected, children in both treatment conditions made significant gains in use of verbal language, results also indicate that when naturalistic communication interventions are used, children may demonstrate gains in areas not specifically targeted. These data are encouraging as they suggest core deficits in autism may be improved as a function of PECS and PRT.

128.57 57 Emotion Perception during An Audio-Visual Emotion Perception Task: Differences Between Forced-Choice and Free Response Formats in Individuals with Autism Spectrum Disorders and Typically-Developing Individuals. S. M. McManus*, A. Rozga, J. L. Zaj, T. Z. King and D. L. Robins, *Georgia State University*

Background: The accurate perception of facial expression and prosody are critical for successful social interactions. When information is perceived from multiple modalities, typically-developing individuals (TD) consistently show a bias toward facial emotion during forced-choice tasks (Massaro et al., 1996; Santorelli & Robins, 2006). Studies have shown that individuals with autism spectrum disorders (ASD) have difficulties understanding emotions expressed by others, even when emotion labels are provided for them (Lindner & Rosen, 2006). Individuals with ASD have also been shown to be less efficient than TD in facial perception tasks with visual-only and combined auditory-visual stimuli (Gepner et al., 1996). In another study, children with ASD are able to infer emotional states when provided with specific prompts, but they do not spontaneously use emotion terms to describe others (Serra et al., 1999). Taken together, these findings suggest that individuals with ASD may possess the ability to accurately interpret and identify emotions portrayed by others, but do not spontaneously look for or evaluate nonverbal cues.

Objectives: The current study investigates whether individuals with ASD show the same pattern of responses as TD individuals on free-response and forced-choice versions of a dynamic audio-visual emotion perception task. In addition, this study examines whether individuals with ASD, like TD individuals, are biased toward information from the visual modality when presented with conflicting emotional information from the auditory modality on a forced-choice format.

Methods: Participants were recruited as part of a larger study. The ASD group included 10 individuals (M = 19.8, range 12-49). The TD group included 8 individuals (M = 15.2, range 9-30). On the forced choice task, participants were presented with an emotion word cue (e.g. happy, angry) and asked to determine whether or not it correctly described the affect portrayed in the subsequent movie clip (i.e., yes/no). During the free response task, participants were presented with stimuli and subsequently asked to label the affect portrayed by the actor using a single emotion word. Only incongruent (i.e. happy face/angry voice) movie stimuli were utilized for this study.

Results: Paired-samples t-tests were conducted. When presented with incongruent movies in the forced-choice format, TD participants showed a strong bias towards the facial expression ($t=3.000$, $p=.020$, $\eta^2=.56$). The ASD group did not demonstrate such bias, instead equally relying on facial expression and prosody ($t=1.432$, $p=.186$, $\eta^2=.19$). When asked to provide one emotion word to describe the actor's affect during a free response task, neither the TD group ($t=.640$, $p=.543$, $\eta^2=.06$) nor the ASD group ($t= -.469$, $p=.651$, $\eta^2=-.03$) showed a bias toward one modality.

Conclusions: Findings suggest that complex emotion perception impairments in individuals with ASD may result from an under-reliance on interpreting facial expressions when asked about a specific emotion. However, this may only be the case in forced-choice emotion perception tasks, which is a format frequently used in emotion research. Neither group showed a modality bias

during the open-response format. Future research should consider potential differences in response formats in order to influence intervention strategies addressing the social difficulties in ASD.

128.58 58 Autistic Traits and Sensitivity to Instruction. C. Hutchins*[1], M. Ota[2] and M. E. Stewart[1], (1)*Heriot-Watt University*, (2)*University of Edinburgh*

Background: Individuals with Autism Spectrum Disorder (ASD) and those high in autistic traits have been shown to be less influenced by contextual information accompanying the percept than controls (Jolliffe & Baron-Cohen, 1999; Noens & van Berckelaer-Onnes, 2008). Recently, Stewart & Ota (2008) investigated auditory speech perception using a Ganong paradigm; a segment identification test using two word-to-nonword Voice Onset Time (VOT) continua (kiss-giss and gift-kift). A significant negative correlation was found between autistic traits and the identification shift that occurred between the continua. As autistic traits increased participants were more likely to respond according to the actual acoustic difference, whereas those that had fewer autistic traits were more likely to respond in the direction of the real word. Pilot studies found variations in phoneme identification patterns as instructions differed.

Objectives: To investigate the extent, effect, and importance of emphasis in instructions when studying aspects of phonological processing and the relationship with autistic traits.

Methods: Twenty-four typically developing adults undertook a phoneme identification task designed to bias responses by providing contextual information immediately following the phoneme offset. Phonemes could be conceptualised as a seven point continuum from /gi/ to /ki/, with those items occurring near the midpoint being ambiguous. Instructions varied by emphasising either the lexical or auditory aspect of stimuli, such that participants' attention would be drawn to those particular properties of the percept. Instructions with a lack of emphasis were also added as a control condition. All participants completed the Autism-Spectrum Quotient (AQ; Baron-Cohen, Wheelwright, Skinner, Martin & Clubley, 2001).

Results: When participants were asked to attend to the acoustic properties of the utterance, mean differences between continua were smaller, such that the lexical bias shown in the typical Ganong experiment was reduced. When asked to attend to the lexical properties, larger mean differences between continua suggested an amplified lexical effect as participants responded in favour of the word over the non-word. This instructional bias was correlated with scores on the AQ.

Conclusions: Marked differences in patterns of phoneme identification between conditions suggest that subtle differences in instruction can bias attentional focus when processing phonological stimuli. This appears to be enhanced in those who score more highly on the AQ, further suggesting that sensitivity to instruction may vary with autistic traits.

128.59 59 Peer-Mediated Intervention for Elementary School Students with Autism Spectrum Disorders: Considering Both the Role of Attributions and Behavior. A. Blakeley-Smith* and S. Hepburn, *University of Colorado Denver School of Medicine*

Background:

Social deficits have been described as the most defining feature of autism (Kanner, 1943) and are noted to cause difficulties across the life span (Seltzer et al., 2003). The socially inappropriate behaviors of elementary school students with autism spectrum disorders (ASD) place them at risk for peer rejection, adjustment difficulties, and problem behavior. Peer-mediated interventions have emerged as an effective means of increasing the social interaction between students with ASD and their typically developing peers. However, without specifically matching intervention strategies to observed deficits both in the students with ASD (e.g., poor social initiation and responding) and their peers (e.g., negative attitudes, poor responding to the peer with ASD), socially meaningful outcomes may not be obtained.

Objectives:

The present study is designed to extend the peer-mediated intervention model by using a two-pronged approach: specifically providing peers with behavioral strategies to facilitate social interaction with the student with ASD while also targeting negative peer attributions through cognitive strategies. The goals of the peer-mediated intervention are: (a) to increase opportunities for positive social interaction

between students with ASD and their peers by identifying school activities that optimize positive social interaction; (b) to assist peers in reframing attributions of the behavior of students with ASD through psycho-education; (c) to train peers in social interaction strategies; and (d) to decrease rejection and problem behavior in selected school activities.

Methods:

The present study uses a multiple baseline across participants design to evaluate the impact of the intervention on the social behavior of three elementary school students with ASD and their peers.

Results:

The present study uses video vignettes of children with ASD as a means of assessing peer attributions based on core social deficits commonly observed in children with ASD. These data are used to individualize the cognitive strategies to target negative attributions for participating peers. These results and strategies will be described. In addition, data obtained from social behavioral coding of peer and student with ASD interaction will be described as an important foundation in determining specific behavioral strategies to employ in peer training. These results and strategies will also be described. Finally, the impact of the intevention will be depicted through a multiple baseline design across participants which will reflect changes in social interaction.

Conclusions:

Given that research suggests that the success of school inclusion may be mediated by the social acceptance and rejection of peers (Odom et al., 2006), examining and modifying negative peer attributions and facilitating positive social interaction among students with ASD and their peers is clearly important. The present study reflects an important next step in the refinement of peer-mediated interventions by using both cognitive and behavioral approaches to specifically reduce rejection and enhance social interaction. Challenges and next steps will be discussed.

128.60 60 UCLA PEERS Program: Predictors of Social Skills in Adolescents with High-Functioning Autism. Y. C. Chang*[1], A. R. Dillon[1], R. W. Ellingsen[2], J. Sanderson[1] and E. Laugeson[1], (1)*UCLA Semel Institute for Neuroscience & Human Behavior*, (2)*University of California, Los Angeles*

Background: Social skills deficits continue to be a struggle as children with Autism Spectrum Disorders (ASD) approach adolescence. Many early intervention programs for children with ASD emphasize social skills training; however, very few of these programs have been developed for older adolescents with ASD. Past research has shown promising results in the effectiveness of social skills training for adolescents with ASD, but no studies to date have examined the characteristics of adolescents with ASD who are benefitting from these programs.
Objectives: This study examines the predictors of positive social skills outcomes from the UCLA PEERS Program, a manualized, evidence-based parent-assisted social skills intervention aimed at improving social skills and friendship quality among adolescents with high-functioning autism (HFA) or Asperger's Disorder (AS).
Methods: Participants included 61 adolescents with HFA or AS, ranging from ages 13 to 17 (M = 14.67 years). Each participant was randomly assigned to either the treatment or the waitlist control group for the UCLA PEERS Program. Adolescents and their parents attended 12-14 weekly 90-minute group treatment sessions. In the adolescent sessions, participants were taught skills such as strategies for joining and maintaining conversations, handling bullying and teasing, being a good host during get-togethers, using electronic communications, and appropriate use of humor. During these sessions, a social skills lesson was taught and followed by role-play exercises for the adolescents to practice their newly learned skill. Concurrent in the weekly parent sessions, parents were given social coaching strategies to assist their adolescents in completing their weekly socialization homework assignments outside of group. Factor associated with parent-reported improvement on a standardized measure of social skills (SSRS) were examined across both groups.
Results: Participants were divided into two groups, based upon parent reports of adolescent social skills improvement on the SSRS following treatment. Among the 46 participants (75.4%)

whose social skills improved, adolescents demonstrated increased knowledge of social skills ($p < .001$), better friendship quality ($p < .025$), and improved self-concept ($p < .005$). Baseline variables that appear to predict increases in social skills following treatment included adolescent self-report of popularity ($p < .025$) and parent-report of social skills before treatment ($p < .001$). Other demographic variables including age, grade, gender, ethnicity, school placement, IQ, and adaptive functioning were not correlated with positive outcomes in social skills.
Conclusions: Baseline social skills were positively correlated with treatment outcome on the SSRS; whereas adolescents' perceptions of their popularity at baseline were negatively correlated with positive social skills outcome. These findings suggest that adolescents who have higher parent-reported social skills scores prior to the intervention may be more likely to show improvement in overall social skills following the PEERS intervention. In addition, adolescents who deem themselves to be less popular prior to the intervention may be more likely to show improvement in social skills following treatment.

128.61 61 Best-Evidence Synthesis of Interventions for Increasing Pro-Social Behavior of Individuals with Autism Spectrum Disorders. B. Reichow*[1] and F. R. Volkmar[2], (1)*Yale Child Study Center*, (2)*Yale University School of Medicine*

Background:

Since the time of Kanner's first description of the syndrome of 'early infantile autism' (Kanner, 1943) major difficulties in social interaction have consistently been identified as a, if not the, central feature of autism. Somewhat paradoxically, social skills were comparatively much less studied than other aspects of autism. However, the last decade has witnessed a steady progression the development and implementation of social skills interventions. These are widely used with individuals of all ages and fall into three general categories: adult mediated (teacher or clinician instruction/therapy), peer mediated (particularly with preschoolers), and combination approaches (social skills groups with peers and an adult present). The focus, theoretical orientation, developmental framework, and empirical support of these models has varied considerably.

Objectives:

This poster presents the findings of a best-evidence synthesis that was conducted to evaluate the empirical evidence supporting social skills interventions designed to increase pro-social behavior of individuals with autism spectrum disorders. We review the empirical basis for social skills interventions, summarize areas of consensus and controversy between methods, and highlight issues particularly in need of research.

Methods:

Six criteria were used to select the studies included in this synthesis: (a) majority of the participants had ASD, (b). interventions designed to improve one or more social behavior were evaluated, (c) at least one social outcome of the participants with autism was evaluated, (d) the evaluation was conducted using true experimental designs, quasi-experimental group designs, single subject research designs, (e). the study was published or accepted for publication with online availability in English in a peer-refereed journal between 2001 and July 2008, and (f) study reports received acceptable or strong methodological rigor ratings on the rubrics outlined in the Evaluative Method for Determining Evidence-Based Practices in Autism (Reichow, Cicchetti, & Volkmar, 2008). Eighty-one reports containing 83 studies were located meeting all inclusion criteria. Analysis of the studies was completed using a multi-step process. First, the studies were categorized into a two-level organizational scheme. Then the delivery agent of the intervention were categorized within age groups. Finally,information pertaining to the characteristics of the research methods, participants, and intervention were analyzed.

Results:

The results of the synthesis will be presented on three levels. First, an overview of the participants, research rigor, and research designs across studies are provided. Second, the characteristics of the methods, participants, and interventions will be synthesized by age group. Finally, the findings of the studies will be synthesized across the different types of intervention. Findings specific to the intervention delivery agent will be discussed with reference to the intervention methods.

Conclusions:

Collectively, the results of this synthesis show there is much supporting evidence for the treatment of social deficits in autism. The synthesis highlights the results of studies that have been conducted using over 800 participants to evaluate interventions with different delivery agents, methods, target skills, and settings. The increasing trend with respect to the number of studies on social skills interventions for individuals with autism confirm addressing the core social deficit in autism has become a priority for researchers.

128.62 62 Parent-Assisted Social Skills Training Program for Young Adults with Autism Spectrum Disorders: The UCLA PEERS Program. A. Gantman* and E. Laugeson, *UCLA Semel Institute for Neuroscience & Human Behavior*

Background:

Among young adults with Asperger's Disorder/High Functioning Autism (AD/HFA), social deficits can lead to significant impairment in daily living, vocational skills, social relationships, and psychological issues. Difficulties in social skills acquisition and generalization are often the most significant challenges for children and adults with AD/HFA. Yet, there is a tremendous void in the treatment research which encompasses transitional youth/young adults with AD/HFA. Few studies have examined the difficulties these young adults endure during this highly socially, emotionally, and physically demanding period of their lives, even though research suggests that the effects of AD/HFA are greatest in adolescence and young adulthood. This period encompasses school transition, finding employment, building social networks, increasing contributions to household, greater involvement in the community, and the development of romantic relationships.

Among the research conducted with this population, findings suggest that only 15% of adults with AD/HFA have friendships with shared enjoyment, and even fewer are married. Social contacts are primarily based on special interests rather than strong/in-depth relationships. Lack of social skills in young adults with AD/HFA may lead to more isolation and thus a lack of interpersonal relationships, vocational difficulties, victimization and exploitation, and increased psychopathology. Moreover, young adults with AD/HFA have higher rates of depression and generalized anxiety.

Possession of good social skills is an important factor in long-term adjustment of individuals with AD/HFA. Research indicates that having one or two best friends is of great importance to later adjustment, can buffer the impact of stressful life events, and correlates positively with self-esteem and negatively with anxious and depressive symptoms.

Social skills training is a well documented intervention strategy for children/adolescents with AD/HFA, yet to date there do not appear to be any evidence-based interventions focused on improving social skills for young adults with AD/HFA.

Objectives:

To assess feasibility of parent-assisted social skills intervention for young adults with AD/HFA.
Methods:

The manualized intervention will consist of an adapted 14-week evidence-based parent-assisted social skills treatment program for transitional AD/HFA youth 18-22 years of age. 20 participants and their parents will participate in the PEERS for Adults Program by attending weekly 90-minute treatment sessions, which will consist of didactic social skills lessons, modeling demonstrations, role-playing exercises and behavioral rehearsal activities. Didactics lessons will target: conversational skills; peer entry/exiting strategies; choosing appropriate friends; planning/implementing get-togethers; handling peer rejection; avoiding peer exploitation/victimization; and resolving conflict with peers.

Results:

Preliminary results of this study, which are forthcoming, are anticipated to reveal that the PEERS for Adults intervention effectively improved the social functioning of transitional youth with AD/HFA and had a positive effect on psychosocial functioning and friendship quality.

Conclusions:

Findings are anticipated to suggest that the use of an adapted manualized parent-assisted social skills intervention is effective in improving the social competence and friendship skills of young adults with AD/HFA.

128.63 63 Social Functioning and Awareness in Adults with Asperger's Syndrome: The Social Stories Task. H. L. Hayward*[1] and M. L. Allen[2], (1)*Unviversity of Oxford*, (2)*Lancaster University*

Background:

Asperger's Syndrome (AS) is characterised by significant impairment in social functioning and social ability, usually present with average or high cognitive ability. Current intervention techniques tend to focus more on young lower functioning individuals leaving high functioning adults with AS to learn and develop techniques on their own. Klin et al. (2007) found severe impairment in adaptive functioning skills in high functioning individuals with ASD suggesting that high intellect can mask actual ability to effectively navigate the social world. Thus, understanding how such individuals understand everyday social situations is paramount in order to design effective coping strategies.

Objectives:

A social stories task based on real-life scenarios was used to assess social functioning and awareness in adults with AS. Specifically, this research investigates whether individuals with AS understand what is appropriate/inappropriate in contemporary social situations. In addition, this projects looks at how self esteem may relate to social ability.

Methods:

15 adults diagnosed with AS (recruited from the NAS) matched on IQ/chronological age to 15 typically developed adults given the Adult Asperger Assessment (Baron-Cohen et al., 2005 – to confirm a diagnosis), the Vineland Social Maturity Scale (VSMS), a self esteem questionnaire and a Social Stories experimental task (SST) developed from Happe's (1994) 'Strange Stories'. The SST covers social domains from Happe's task including Irony, Sarcasm, Lie and four novel domains Rudeness, Morality, Disability, Appearance. The participants were given 40 short scenarios (four in each domain) depicting appropriate/inappropriate social interactions and asked to judge whether the characters did something acceptable/unacceptable. Participants were then asked to justify these responses.

Results:

There was significant difference between groups on measures of self esteem with the AS group affected by feelings of lower self esteem when perceiving themselves rather than how others view them ($t = -2.021$, $p = 0.05$). The AS group was significantly impaired on all areas of social functioning task and this impairment highly correlated with social age (from VSMS). The AS group were also more likely to accept the inappropriate response to a story ($F(1, 29) = 26.526$, $p = 0.005$), and reject the appropriate. Within the AS group, a significant negative correlation was found between overall understanding of the social scenarios and both rejection of appropriate response ($r=.45$, $p<0.05$) and the Autism Quotient gained from the AAA ($r=-.45$, $p=0.05$). All four novel domains came out as significantly positively related to overall understanding of the social scenarios. When asked to give justifications the AS group displayed a desire to change original answer suggesting these individuals may consider a social scenario more carefully when asked to reflect upon it.

Conclusions:

This study confirms prior research showing overall deficit in social skills functioning, and importantly extends this finding to novel, ecologically valid, domains. This project also confirms the SST as a relevant and useful tool for assessing current social and adaptive functioning in high functioning adults with AS, and provides an understanding of how individuals with AS understand social situations as appropriate or inappropriate. Thus, these findings have implications for intervention and individual social skills training.

128.64 64 A Comparison of Asperger's Disorder and High Functioning Autism: Are Diagnostic Boundaries Meaningful/Useful?. R. Bernier*, J. Varley, K. M. Venema, K. Stamper and S. J. Webb, *University of Washington*

Background:

The use of accurate and appropriate subtypes of pervasive developmental disorders is necessary across scientific, clinical, and educational settings. Since the inclusion of Asperger Syndrome (AS) as a diagnostic entity, a number of studies have examined the clinical presentation of AS relative to Autistic Disorder with cognitive abilities in the average range (HFA). While several studies have identified differences between AS and HFA in a variety of domains (perinatal factors, cognitive profiles, motor ability, etc), the validity of the

current diagnostic subtypes remains under debate.

Objectives:

The purpose of the current study is to compare the diagnostic subtypes of AS and HFA using parent report of behavioral symptoms and neurophysiological measures of social information processing.

Methods:

In a sample of children with continued ongoing recruitment (aged 6-18 years; mean = 10.6 years; all males) and a sample of adults (mean age = 22.3 years; all males), meeting ASD criteria on the ADI and ADOS and having a full scale IQ in the normal range, individuals were identified as AS (children: N=13; adults: N=15) or HFA (children: N=20; adults: N=13) using strict DSM-IV criteria by an experienced clinician. In the sample of children, parent report of behavior and functioning (CBCL competency scales and vineland) was examined to examine differences between diagnostic groups. In the sample of adults, EEGs were collected in response to pictures of faces and houses and in response to pictures of familiar and novel faces. To examine differences between diagnostic groups, latency and amplitude of EEG response was assessed.

Results:

In the sample of children, significant differences were found on verbal IQ between groups with the AS group performing significantly better ($p<.01$) than the AD group. No differences were found in the non-verbal domain. After controlling for verbal IQ, significant differences were found between groups on the school problems subscale of the CBCL with the AS group performing in the typical range and the AD group performing in the clinical range ($p<.05$). No differences were found between the AS and AD groups on the social and activities subscale of the CBCL competency items or Vineland scores. In the sample of adults, no differences were found on verbal and nonverbal IQ. The AS group showed faster processing of both face and house stimuli in the right hemisphere and the HFAD showed faster processing in the left hemisphere ($p<.05$). Further, while similar latencies were noted at an early negative going ERP component in response to familiar faces, the HFAD group showed faster processing of novel faces than the AS group ($p<.05$).

Conclusions:

The preliminary findings in children suggest that meaningful differences between boys with AS and AD do exist and that despite typical school functioning and enhanced verbal IQ skills in children with AS, adaptive functioning remains significantly impaired. The findings in adults suggest processing novel social information may be different for males with AS compared to HFAD and support the conclusion that meaningful differences exist between subtypes and that these differences manifest in neurophysiological responses to social stimuli.

128.65 65 A Scale to Assist the Diagnosis of Autism Spectrum Disorders in Adults: Results of An International Multi -Center Study. E. R. Ritvo*[1], R. A. Ritvo[2], M. J. Ritvo[3] and D. Guthrie[1], (1)*UCLA School of Medicine*, (2)*Yale University School of Medicine*, (3)*Harvard Westlake School*

Background: An initial version of The Ritvo Autism Asperger Diagnostic Scale (RAADS) contained 78 questions. Published data demonstrated that it was valid, reliable, highly sensitive, and highly specific in a limited number of subjects. Questions assess developmental pathology in three symptom areas (language, social relatedness, sensory-motor responses per DSM-IV TR). The new 80-item version reported herein was developed after critical review led to the addition of two questions and wording clarifications. Objectives: To present initial findings of an international multi-center standardization study of the new 80-item version of the scale. Methods: Adult ASD subjects at eight university medical centers (three in Australia, four in the USA, one in Canada) were diagnosed by research criteria which included: 1) a clinical interview, 2) a Constantino SRS Scale, 3) an ADOS Scale to assess validity, 4) a standardized IQ test, 5) repeat testing to asses reliability. Comparison subjects were: 1) Volunteers without a DSM IV -TM diagnosis, 2) Volunteers who had a current DSM IV-TM diagnosis other than an autism spectrum disorder. Translations that take into account cultural variations, core syndrome regardless of language, and will permit standardization of results and assessment of validity and reliability are in early stages of development. They are being conducted at the

Karolinska Institute, Stockholm, Sweden and at Nagoya, Japan. Results: The results to date demonstrate that the new 80 item version of the scale is highly valid and highly reliable (sensitivity and specificity >90%, test retest data show no significant change in scores over a one year interval) . Conclusions: The scale can assist clinicians diagnosing autism spectrum disorders in adults.

128.66 66 Appropriateness of Standardized Testing to Determine Behavioral Treatment Eligibility of Children with ASD. R. Stock*, P. Mirenda, S. Jull and K. Bopp, *University of British Columbia*

Background: Frequently, behavioral intervention programs for children with ASD are faced with the question of which children to admit for treatment because of limited resources. Some programs require standardized assessments of cognitive, language, and/or adaptive behavior functioning in order to make intake decisions; children who are "untestable" on one or more such measures may not be admitted for treatment. Thus, it is important to know whether or not "testability" at baseline is a valid measure of a child's potential response to treatment. A measure used in many assessment batteries is the Peabody Picture Vocabulary Test-III (PPVT-III), which requires a child to point to one of four pictures on a page in response to a spoken word cue.

Objectives: The primary goal of this exploratory study was to examine changes in children's testability on the PPVT-III over three time points, starting with assessment prior to the initiation of early intervention (T1). A secondary goal was to determine whether there were differences on measures of aberrant behavior, adaptive behavior, and autism severity over time between children who were and were not testable on the PPVT-III at T1.

Methods: Sixty-nine children with ASD (84% males) were assessed at T1 (mean CA=50 months) and both 6 months (T2) and 12 months (T3) thereafter. Single word receptive vocabulary was measured with the PPVT-III. The sample was divided into children who were unable to complete the PPVT-III at T1 and those who attained a raw score score ≥1. Independent t-tests were used to examine whether there were differences between the two groups on subscales of the Temperament and Aberrant Behavior Scale (TABS), Vineland Adaptive Behavior Scale adaptive behavior composite (VABS ABC), and/or Childhood Autism Rating Scale (CARS).

Results: At T1, 51% of children (n=35) were untestable on the PPVT. There were significant differences ($p<.001$) between the testable and untestable groups on the TABS detached and under-reactive behavior subscales, CARS, and VABS ABC, with the untestable group showing more evidence of aberrant behavior, higher autism severity, and lower adaptive behavior. At T2, 29% of the children were untestable on the PPVT-III, a decrease of 22%. Again, significant differences were found between the two groups that were identical to T1. At T3, 25% of the children were untestable on the PPVT-III, a decrease of only 3%. The pattern of between-group differences identified at T1 continued to be evident.

Conclusions: The results indicate that a significant number of children who could not point to pictures on demand at T1 were able to do so after 6 months of behavioral intervention. The children who continued to be untestable at all time points presented with more detached and under-reactive behavior, higher autism severity, and lower adaptive behavior scores. It appears that the persistently untestable children were those who might be expected to make the least progress in behavioral intervention over time. The results suggest that a 6-month trial of behavioral intervention would be appropriate prior to determining which children are likely to benefit from this form of treatment.

128.67 67 Factors Related to False-Positive Diagnoses by Community Sources. E. H. Dohrmann*, A. C. Vehorn, A. G. Nicholson, M. M. Kaminski and Z. Warren, *Vanderbilt University*

Background: As genetic research continues to attempt to amass large numbers of children and families for analysis, more and more children that have received diagnoses from community sources are being recruited for potential participation. Phenotypic assessment of these children utilizing gold standard assessment tools such as the Autism Diagnostic Observation Schedule (ADOS), Autism Diagnostic Interview-Revised (ADI-R), as well as ultimate clinical diagnosis (CBE), commonly find that a large percentage of children referred by community sources do not, in fact, meet criteria for an ASD.

Objectives: In the current report we analyzed factors commonly associated with community referrals of false-positive ASD cases.

Methods: The family cases analyzed were participants in the Vanderbilt site of the Simons Simplex Collection. Each family had one child with either a previous, community-based diagnosis of ASD or an elevated score on the SCQ (i.e., >= 9). The family then completed a battery of questionnaires, a thorough medical history interview, and a series of cognitive and diagnostic assessments, including an ADOS and an ADI-R. Each case was then reviewed by at least one licensed clinician and clinical best estimate diagnosis was issued. Files of cases not meeting diagnostic criteria for ASD were reviewed and variability associated with 1) administered measures and/or 2) important medical and environmental factors was explored.

Results: Of the 85 families completing our assessment protocol, 12 recruited children did not receive an ASD diagnosis (14.11% of the sample). The age range for these children was 4 to 12 years. 41.6% of these subjects were female. 33.3% were home-schooled; 66.7% had conflicting cursory diagnoses by medical professionals using measures other than the ADOS/ADI-R; 50% met criteria on the ADI-R and other parent report measures, but not on face-to-face measures; 25% met criteria on both the ADI-R and ADOS but did not warrant a CBE of ASD; and 16.6% expressed significant external pressures (i.e. state financial support or internet self-diagnosis) to secure an ASD diagnosis.

Conclusions: Several factors were prominent in children diagnosed with ASD in the community or meeting thresholds solely on a parent referral checklist who ultimately did not meet diagnostic criteria of ASD using gold-standard assessment practices. Specifically, families with children with limited exposure to traditional school settings, receiving a diagnosis of ASD from an M.D., and children with parents who generated self-diagnoses were common in our sample. These findings highlight the importance of standardized assessment tools in combination with clinical expertise in order to control for potential false-positive cases in large scale recruitment endeavors such as genetic repositories. The trends reported here also may have implications for recruitment and screening methods chosen by researchers attempting to access participants with ASD from broader community settings.

128.68 68 Specifying Pervasive Developmental Disorder – Not Otherwise Specified: The Case for 'Atypical Autism'. W. Mandy*[1], L. Slator[2], M. Murin[2] and D. H. Skuse[3], (1)*University College London*, (2)*Great Ormond Street Hospital for Children*, (3)*Institute of Child Health*

Background: It is an unfortunate paradox that Pervasive Developmental Disorder – Not Otherwise Specified (PDD-NOS) is both the most common and the least satisfactory diagnosis on the autistic spectrum. Its inter-rater reliability is unacceptably low, even amongst experienced clinicians. It has not been formally operationalised in DSM-IV-TR, and is effectively a 'catch-all' diagnosis, introduced by necessity in response to symptom constellations that fail to meet more rigorous criteria. PDD-NOS in its current form cannot be considered a useful diagnostic category, as it is not reliable and is unlikely to communicate with precision about an individual's impairments, the source of their difficulties or their prognosis. As such, PDD-NOS has been described as 'a work in progress' and calls have been made for its more specific delineation. Accordingly, attempts have been made to identify homogenous sub-groups within PDD-NOS. It has been reported that around half of people with PDD-NOS have a specific symptom pattern involving significant impairments in reciprocal social interaction and communication, in the absence of repetitive and stereotyped behaviour. Szatmari and colleagues have suggested the ICD-10 term 'atypical autism' (AA) be used as a specific descriptor for this group. Whilst a number of commentators have endorsed this suggestion, fewer than 30 people with AA have been phenotypically described in the literature, making it difficult to judge its nosological value.

Objectives: To assess the validity of AA using the framework set out by Kendler for establishing psychiatric diagnoses. Specifically we sought to discover if AA has 'concurrent validity' by attempting to differentiate it from autism according to: (1) Core autistic features; (2) associated autistic features; (3) functional impairments commonly associated with autism.

Methods: Participants comprised 567 children consecutively diagnosed with a PDD at two children's hospitals specialising in the assessment of high-functioning autism. Multi-informant (parent, teacher and child) data were collected

using standardised measures (3Di, ADOS, Strengths and Difficulties Questionnaire, WASI). AA (n=228) individuals were compared to those with the full triad of autistic impairments (n=339).

Results: Thirty-nine percent of our PDD sample met criteria for AA. Compared to people with autism, the AA group showed milder social communication difficulties, but the overall pattern of these difficulties was similar in both groups. There were no group IQ differences. The AA group had fewer associated features of autism; showing less sensory sensitivity, fewer eating difficulties, better sleep, superior motor skills and fewer ADHD symptoms. Those with AA showed similar conduct and emotional difficulties to those with autism (home and school), but were less impaired in their peer relations.

Conclusions: 'Atypical Austism' as defined by Szatmari and colleagues is the most common group on the autistic spectrum, with a specific pattern of core PDD symptoms. Crucially, AA can be distinguished from full autism according to features independent of diagnostic criteria, and these differences are not attributable to IQ. Despite their lack of repetitive behaviours, children diagnosed with AA will need similar levels of support as those with full autism syndrome.

128.69 69 Deconstructing the PDD Clinical Phenotype: Internal Validity of the DSM-IV. L. Lecavalier*[1], K. Gadow[2], C. DeVincent[2] and M. Edwards[1], (1)*Ohio State University*, (2)*State University of New York*

Background: Current diagnostic and classification systems conceptualize pervasive developmental disorders (PDDs) in terms of impairments in social interaction, communication, and repetitive-restricted behaviors. Empirical studies of the structure of PDD symptoms have challenged this three domain model of impairment. For example, some authors have proposed a single dimension to characterize PDD symptoms, others have proposed two-dimensional models consisting of social-communicative and repetitive-restricted behaviors, and yet others have proposed models with more dimensions.

Objectives: To assess the internal validity of the DSM as a conceptual model for describing PDD, while paying particular attention to certain subject characteristics. In order to overcome methodological shortcomings of previous studies, we examined DSM-IV symptoms from all three core PDD dimensions, included a large sample of PDD children with the full range of symptom severity, and assessed competing models with confirmatory factor analysis (CFA). We examined the impact homogeneous subgroups (based on age, IQ, and PDD subtype) had on model fit.

Methods: Parents and teachers completed a 12-item DSM-IV-referenced rating scale for 3-to-12 year old clinic referrals with a PDD. The sample consisted of 730 children aged 3 through 12 years (mean=7.1; SD=2.5) and was predominantly male and Caucasian. Using DSM-IV criteria, clinical diagnoses were made by an expert clinician. All children met DSM-IV criteria for autistic disorder, Asperger's disorder, or PDDNOS. Ratings were submitted to CFA and different models were assessed for fit. Analyses were first conducted on the entire sample and then based on age (preschool, n=229 vs school age, n=501), PDD subtype (autism n=254, Asperger's, n=154, and PDDNOS, n=322), and in 6-12 years olds with IQ>70 (n=263). Three models were tested in every subsample: a one-factor model, a two-factor model consisting of the eight social-communication items and four restricted/repetitive behavior items, and a three-factor model representing the DSM-IV triad of impairments.

Results: Measures of fit indicated that the three-factor solution based on the DSM was superior to other models. The one- and two-factor models yielded poor fit for both informants. Fit indices varied according to the rater, child's age, PDD subtype, and IQ. Overall, factor loadings were high for both parents and teachers. Subgroup analyses impacted indices of fit, especially for parent data. For instance, models for school age children had better fit than observed with preschoolers (RMSEA=.075 vs .098) and improved if only children with IQ>70 were included in the analyses (RMSEA=.057). In terms of PDD subtypes, fits were best for Asperger's disorder (RMSEA=.039) and poorest for autism (RMSEA=.095). There was less differentiation across subject characteristics with the teacher data.

Conclusions: Results clearly indicated that the three-factor solution provided better fit to the data than the one- and two-factor solutions previously reported in the literature. Regardless of subject characteristics, the three-factor solution

always resulted in better fit indices than the other models tested. The current data also showed that subject characteristics impacted fit. More research needs to be done before discarding current classification systems. Subject characteristics, modality of assessment, and procedural variations in statistical analyses impact conclusions on the structure of PDD symptoms.

128.70 70 Mental Health Aspects of Autistic Spectrum Disorders. N. Skokauskas*, L. Gallagher, S. Brennan and M. Law, *Trinity College Dublin*

Background: autism spectrum disorders (ASD) classified as pervasive developmental disorders in ICD-10 and DSM-IV, occur along a broad continuum of severity with impairments in social interactions, communication and behaviour. For the person with the condition the cause of mental health difficulties is quite often put down to the autism and in the relatives it is attributed to the stress of living with a person with autism. However co-morbid psychiatric diagnoses can complicate the management of individuals with autism and accurate, reliable diagnosis of co-morbidities is of major importance. When problematic behaviours are recognized as manifestations of a co-morbid psychiatric disorder, more specific treatment is possible.

Objectives: to examine patterns of co-morbid and associated psychiatric problems in children with ASD and their parents.

Methods: Inclusion criteria for the study are diagnosis of autism based on the Autism Diagnostic Interview-Revised (ADI-R), a diagnosis of autism or autism spectrum disorder based on the Autism Diagnostic Observational Schedule (ADOS) and IQ or score greater than 35. Participants were recruited through Child and Adolescent Mental Health Clinics, Specialist Autism Clinics, Special Schools, Advocacy groups and individual clinician referral. In addition to the ADI-R and ADOS the Child Behavior Checklist (CBCL) and the Brief Symptom Inventory (BSI) were administered. The CBCL for ages 6-18 was used to obtain standardized parents' reports of children's social competencies and behavioral/emotional problems. Parents reported their own current level of psychological distress using the BSI.

Results: So far data has been collected from 72 parents of children age range 8–17. The mean IQ score was 75 and the mean age was 12.6 years; 88% were male. Results of the CBCL revealed that majority of parents reported their child as having either internalizing (clinical range: 72.4%; borderline range: 21.4%) or externalizing problems (clinical range: 19.2%; borderline range: 17.1%). Clinically significant difficulties were detected for the ADHD CBCL DSM orientated subscale. Borderline clinically significant means were detected for CBCL anxiety and affective DSM orientated subscales. Parental mean age was 50.1 years. The presence of BSI T-scores greater than 63 on two or more subscales indicates possible psychopathology. Based on this criterion 29% of fathers and 32.5% were diagnosable with psychopathology, obsessive-compulsive and interpersonal sensitivity being most common. Based on BSI Global Severity Index 31% of fathers and 24% of mothers produced scores that were sufficiently severe to suggest a diagnosis of psychopathology. The BSI indices didn't significantly correlate neither with CBCL internalising nor with externalising scores.

Conclusions:

1. The majority of children diagnosed with autism had some internalizing problems and reached clinically significant levels on ADHD CBCL DSM orientated subscale.

2. Based on BSI up to one third of parents were diagnosable with psychopathology, Obsessive-Compulsive and Interpersonal Sensitivity being most common. .

3. Based on an absence of correlation between BSI scores and CBCL scores it could be postulated that parental psychological distress wasn't significantly associated neither with externalizing nor with internalising problems in their children and did not influence the reporting of symptoms in the children.

128.71 71 Maladaptive Behaviours and Associated Characteristics within Individuals with Autism and Intellectual Disability. K. Wells*[1], A. Perry[2], A. Levy[1] and N. Luthra[1], (1)*York University*, (2)*Thistletown Regional Centre*

Background:

Maladaptive behaviours have been referred to by many different labels, including; problem behaviour, aberrant behaviour, and challenging behaviour. All of these descriptors are umbrella terms for a collection of specific behaviours thought to be dangerous, disruptive, threatening,

or harmful to one's self or others. Generally, the intellectual disability literature has focused on three specific forms of maladaptive behaviour; aggression, self injurious behaviour, and stereotyped behaviour (Dawson, Matson, & Cherry, 1998).

It has been suggested that among individuals with intellectual disabilities the rates of those engaging in some form of maladaptive behaviour may be as high as 50% (Atkinson, Feldman, & Condillac, 1998), but rates vary considerably across studies, in large part because of differences in the way maladaptive behaviour is defined and measured. The situation is considerably more complicated when the individual also has autism, since the maladaptive behaviours may be attributed to the autism (e.g., agitation), but also because symptoms of autism may appear to mimic other forms of psychopathology or maladaptive behaviour (e.g., delayed echolalia may appear psychotic, lack of social initiation may mimic depression).

Age, cognitive ability, gender, and communicative skills have all been found to correlate with the occurrence of maladaptive behaviours in individuals with an intellectual disability (McClintock, Hall, & Oliver, 2003). It is unclear the degree to which certain types of maladative behaviour may be a function of degree of intellectual disability and severity of autism when these disorders are comorbid.

Objectives:

Very few studies have examined the characteristics associated with maladaptive behaviours within individuals who have comorbid autism and intellectual disability. This is despite the fact that both autism and impaired cognitive functioning have been associated with higher levels of maladaptive behaviours. The purpose of this study is to examine those characteristics that may be associated with maladaptive behaviours within such a population.

Methods:

This was a file review study at a school and residential setting for individuals with autism in Toronto, Ontario, Canada. The sample includes 60 participants ages 8 to 41. The Vineland Adaptive Behaviour Scales – 2nd Edition was used as a measure of the participants' level of engagement in maladaptive behaviours, as well as a measure of their adaptive behaviours. Measures of cognitive skills, communication, and severity of autism were also administered to the participants. All measures were given within the context of routine clinical assessments by a team of trained clinicians.

Results:

Data analysis is currently underway. Four maladaptive scores were derived from the Vineland-II: internalizing, externalizing, other, and critical items. Each of these will be examined in relation to age and gender as well as the following developmental and diagnostic variables: severity of autism, verbal and nonverbal mental age, expressive and receptive communication, daily living skills, and social skills.

Conclusions:

Conclusions will focus on the conceptualization and clinical implications of the results regarding maladaptive behaviours in this population, including the risk of possible misinterpretations of scales or items in children with low cognitive levels and severe autism.

128.72 72 Group Cognitive Behavior Therapy for Children with High-Functioning Autism Spectrum Disorders and Anxiety: a Randomized Trial. J. Reaven*, A. Blakeley-Smith, K. Ridge and S. Hepburn, *University of Colorado Denver School of Medicine*

Background: Individuals with developmental disabilities are at increased risk for developing anxiety disorders and children with high-functioning autism and Asperger Syndrome are at even greater risk for developing significant anxiety symptoms (Bellini, 2004; 2006; Brereton, Tonge & Einfeld, 2006; Gilliot, Furniss, & Walter, 2001). Anxiety can be a debilitating disorder as symptoms can markedly interfere with an individual's ability to participate in home, school and community activities (Velting, Setzer & Albano, 2004). Cognitive-behavioral therapies (CBT) are frequently used for children with anxiety symptoms in the general population with good success (Compton et al. 2004; Walkup et al. 2008). Given the common co-occurrence of anxiety and autism spectrum disorders (ASD), it is surprising that so few treatment studies of dually diagnosed persons exist in the literature. In fact, research studies using randomized controlled

trials have typically excluded children with pervasive developmental disorders.
Objectives: To conduct a randomized, controlled study of the treatment package, by comparing treatment as usual (e.g.,wait-list control) with parent/child participation in the 12-week intervention. Impact of the treatment package will be assessed by examining the reduction in severity of anxiety symptoms in children.
Methods: Children ages 8-14 were recruited from the Autism Clinic of JFK Partners, University of Colorado Denver and through word of mouth in the Denver community. Criteria for inclusion: 1) current clinical diagnosis of an autism spectrum disorder, 2) exceeding criteria for ASD on the ADOS, 3) exceeding criteria for ASD on the SCQ, 4) presenting with clinically significant symptoms of anxiety on the Anxiety Disorders Interview Schedule – Parent Version (ADIS-P), and 5) Verbal IQ of 80 or higher. Children and their parents participated in the 12 week group treatment. Multiple outcome measures were used including the Clinician Severity Rating (CSR) from the ADIS-P, that was obtained from an independent rater, blind to condition. Other outcomes measures included the Screen for Child Anxiety Related Disorders (SCARED) – parent and child report, the Children's Automatic Thoughts Scale (CATS), and measures of parental anxiety.
Results: Forty-four children with ASD and their parents participated in the study. Preliminary findings indicated that there were no pre-treatment differences on measures of IQ, age, autism severity and clinical anxiety symptoms. Data regarding independent clinician severity ratings, anxiety diagnostic status, parent interference ratings and functional outcomes will be presented. Preliminary analyses reflect promising changes in symptoms of social phobia and specific phobia from pre to post-treatment.
Conclusions: Preliminary findings suggest that group CBT treatment, with parent participation, may be effective in decreasing anxiety symptoms in children with ASD. Limitations of this study include small sample size, as well as the lack of a social attention control group.

128.73 73 Differentiating Autism Spectrum Disorder (ASD) Subtypes Using Estimates of IQ and Language. C. Chrysler*, P. Szatmari and E. Duku, *McMaster University*

Background: While it is possible to reliably and accurately differentiate autism from non-ASD children, the differentiation of Asperger syndrome (AS) from autism is much more difficult. Although DSM-IV states that children with AS do not have clinically significant cognitive or language delay, the operationalization of these criteria are difficult to implement and evaluate.

Objectives: To evaluate the ability of a diagnostic algorithm employing both estimates of IQ and language to accurately differentiate Asperger syndrome from autism.

Methods: The sample consisted of 347 individuals with autism, and AS referred to a genetic study. Inclusion criteria were any child with an ASD but without a primary genetic or medical syndrome. All subjects were assessed using available clinical records, ADI-R, ADOS, a non-verbal IQ assessment (the Leiter International Performance Scale) and the Vineland Adaptive Behaviour Scales (VABS). Each individual was given a best estimate (BE) diagnosis based on clinical records and the above information. Receiving operating characteristic curves (ROC's) were used to estimate the score on the non-verbal IQ test and the Communication scale that best differentiated AS from autism. Using these scores, a new diagnostic algorithm was devised combining the Leiter and VABS Communication scores and was compared to the BE diagnosis. Estimates of sensitivity, specificity and positive predictive value were calculated.

Results: ROC curves identified a score of 80 on the Leiter and 75 on the VABS Communication Scale as the estimates that best differentiate autism from AS (area under the curve=0.80 and 0.87 respectively). Combining both scores as categorical thresholds gives a sensitivity of 0.64, a specificity of 0.85 and a positive predictive value of 0.51.

Conclusions: To differentiate AS from autism, researchers will have to use supplementary information in addition to the ADI-R and ADOS. Using the thresholds employed here, estimates of sensitivity and specificity are quite good but because of the low prevalence of AS in this sample, the positive predictive value is only moderately high. This will be a problem for any diagnostic algorithm that attempts to distinguish AS from autism.

128.74 74 Angry Faces Lead to Less Facilitation of Conditioned Learning in High-Functioning ASD Than in Comparison Groups. S. E. White*, J. Dana, A. Cariello and M. South, *Brigham Young University*

Background: Conditioned learning tasks provide a relatively direct behavioral test of basic amygdala function, and could be used to describe fundamental parameters of amygdala impairment in Autism Spectrum Conditions (ASC). However, the few previous studies of conditioned learning in individuals diagnosed with ASC have reported mixed findings related to the type and degree of impairment on conditioned learning tasks.

Objectives: We designed our study to extend previous studies of conditioned learning in ASC in two key ways: first, we included a lengthier extinction period in order to better examine the time it takes to learn and then to extinguish the new learning (which involves amygdala and orbitalfrontal cortex); second, we manipulated the emotional valence of the conditioned stimulus to compare the facilitation of social/emotional meaning on learning, across ASC and comparison groups.

Methods: Four groups of 15 individuals (two ASC and two comparison groups) completed a simple conditioned learning task that used a 1000ms white noise burst as the unconditioned, aversive stimulus. Two groups (one ASC, one comparison) did the task using neutral, colored squares as the conditioned stimuli (CS); the other groups did the same task but with the colored squares replaced by angry faces. Dependent measures were the difference scores in galvanic skin response (GSR) and heart rate (HR) in response to the safe (non-reinforced) CS versus the threatening (followed by the white noise) CS.

Results: The ASC groups did show conditioned learning in GSR and HR measures, but this learning was significantly slower than the comparison group (i.e., the peak difference score occurred later in the task); extinction was also intact but, subsequently to longer initial learning, also took longer to extinction. In the comparison group, the face stimuli facilitated conditioning as evidenced by a) faster conditioning (peak occurred earlier in the task); b) stronger conditioning (larger peak magnitudes of difference between threat and safe conditions); and c) prolonged activation to the threat stimulus, which delayed extinction. The ASC group, however, demonstrated significantly less facilitation by the face stimuli, showing a response more similar to that evoked by the more neutral colored squares.

Conclusions: We extended research regarding basic behavioral mechanisms of amgydala function in ASC by allowing more time for the conditioned response to occur, and by manipulating the influence of stimulus type in conditioned learning experiments. Our findings suggest that amygdala impairment in ASC may reflect more widespread difficulties elsewhere in the brain, or in connectivity to other brain systems, rather than primary dysfunction in the amygdala itself. That is, fundamental amygdala function (necessary for conditioned learning) is intact but is moderated by other factors of learning speed and social perception.

128.75 75 Is Autism a Unitary Construct? Factor Structure of the Childhood Autism Rating Scale. A. Levy*[1], K. Wells[1], A. Perry[2], J. Dunn Geier[3] and N. L. Freeman[4], (1)*York University*, (2)*Thistletown Regional Centre*, (3)*Children's Hospital of Eastern Ontario*, (4)*Surrey Place Centre*

Background:

The Childhood Autism Rating Scale (CARS; Schopler, Reichler & Renner, 1988) is a behaviour observation scale in which a trained observer rates the child's behaviour on 15 dimensions or symptoms that are related to autism. The measure produces a total score which places the child into one of three categorical diagnoses: not autism, mild/moderate autism or severe autism. This measure has been shown to have important clinical and research utility and is widely used in the diagnosis, treatment planning, and treatment evaluation of children with Autism Spectrum Disorders (ASDs; Magyar & Pandolfi, 2007; Perry, Condillac, Freeman, Dunn Geier & Belair, 2005; Weiss, 1999). Three studies have examined the underlying factor structure of the CARS. DiLalla and Rogers (1994) found that the CARS items loaded onto three separate factors. In their 1999 study Stella, Mundy and Tuchman, study found a five-factor solution, while Magyar and Pandolfi (2007) found four factors. The varying results in these previous studies may be accounted for by differences in their sample characteristics, including; sample size, ages, and diagnoses. The present study examined this issue in a very large multi-site sample.

Objectives:

The underlying factor structure of the CARS was investigated in a large sample of individuals diagnosed with an ASD. This analysis was intended to help determine whether, according to the CARS, there is symptom coherence across

individuals with autism, indicating a general autism factor or whether there are distinct and independent groups of symptoms as previous research on this measure has suggested. This study will further help to elucidate the underlying dimensions of the clinically defined syndrome of autism.
Methods:
This was a file review study involving multiple settings across Ontario, Canada. The CARS was administered to the participants within the context of routine clinical assessments by a team of trained clinicians who have demonstrated high interrater reliability. Data were complied and analyzed for 958 participants.The participants were separated into two groups based on age.
Results:
The results suggest that for the older group of 130 adolescents and young adults with ASD (mean age of 10.42 years) the 15 items of the CARS load onto three separate factors. However, it was found that for the younger group, which was composed of 828 younger children with an ASD (mean age of 4.33 years), the CARS items load onto two factors. Specific items loadings for each factor will be reported and the results compared to those from the previous CARS factor analytic studies. In addition, factor scores will be examined as a function of cognitive level.
Conclusions:
These results suggest that the characteristics of autism, as measured by the CARS, may be different in adolescents and young adults than in younger children and that autism is not necessarily a unitary construct. Possible explanations for these findings will be discussed.

128.76 76 Gender Differences in Symptom Presentation, Emotional Comorbidities and Social Cognition in Higher Functioning Children with Autism. N. Kojkowski*[1], L. Mohapatra[1], C. Hileman[1], P. C. Mundy[2] and H. A. Henderson[1], (1)*University of Miami*, (2)*UC Davis*

Background: Given the gender ratio of 4:1 for autism spectrum disorders, females tend to be underrepresented in research samples so little is known about the specific diagnostic and treatment needs of girls with autism. Gender differences in symptom expression and patterns of comorbidity have important implications for both diagnosis and intervention.
Objectives: To investigate the associations between gender and symptom presentation, social cognition, and emotional comorbidity in a sample of HFA children and a sample of gender, age, and IQ-matched typically developing children.
Methods: Preliminary results are reported on forty-four children (22 HFA (11 female); 22 comparison (11 female). Parents completed the Social Communication Questionnaire and each participant completed the Behavioral Assessment Scale for Children (BASC) self report, Multidimensional Anxiety Scale for Children (MASC) and Strange Stories. Dependent variables of interest were anxiety and depression on BASC as well as the MASC total score and Strange Stories.
Results: Preliminary analyses revealed a trend for an interaction between diagnostic group and gender on the SCQ total score, $F(1,38) = 3.97$, $p = 0.055$. Specifically, HFA males were reported as more symptomatic than HFA females, whereas gender was unrelated to symptom scores within the comparison sample. Additionally, analyses indicated a significant main effect of gender on anxiety, $F(1, 29) = 8.77$, $p < 0.05$ and depression $F(1, 29) = 6.40$, $p = 0.02$ with the BASC-SRP, such that females, regardless of diagnostic status, endorsed more internalizing problems than males. Additionally, there was an interaction between diagnostic group and gender on the MASC anxiety total score, $F(1, 29) = 5.30$, $p = 0.03$. Post hoc analyses revealed that HFA females endorsed more problems with anxiety compared to HFA males and all children in the comparison sample on all three subdomains Physical Symptoms, Harm Avoidance and Social Anxiety. Finally, on the Strange Stories task, HFA females performed significantly better than HFA males, and just as well as the comparison sample, $F(1, 27) = 5.45$, $p < 0.03$.
Conclusions: These data suggest that while still meeting diagnostic criteria, HFA females are perceived by their parents as less impaired than HFA males. However, they also self-reported high levels of internalizing symptoms. Given their relatively in tact social cognitive skills, it may be that HFA females are more aware of others' perceptions, sensitive to their own difficulties, and therefore present as less classically symptomatic in the social domains. This increased sensitivity, may however result in increased internalizing symptoms. The results will be discussed with reference to implications for gender-specific diagnostic and intervention strategies.

128.77 77 Phenomenology of Anxiety and Fears in Clinically Anxious Children with Autism Spectrum Disorders. L. K. Kimel*[1], D. N. McIntosh[2] and S. Hepburn[3], (1)*University of Denver and University of Colorado Denver, School of Medicine*,

(2)*University of Denver*, (3)*University of Colorado Denver School of Medicine*

Background: Children with autism spectrum disorders (ASD) are at increased risk for developing anxiety disorders in childhood compared to typically developing children and to children with other developmental disabilities.

Objectives: Currently, many of the treatments that have been effectively used with children with clinical diagnoses of anxiety disorders, without a developmental disability (AD), are being applied and modified for children with ASD. However, there is a lack of research on the ways in which anxiety disorders may be similar and different in clinically anxious children with ASD compared to children with AD. It is important to make this comparison so that we can develop appropriate models for understanding the influence of the core symptoms of ASD on the development of anxiety disorders, and then further develop intervention programs that target the types of anxiety symptoms that clinically anxious children with ASD display.

Methods: Anxiety symptoms in 19 children with ASD and anxiety disorders were compared to anxiety symptoms in 18 children with AD, matched on chronological age and verbal IQ. All participants were treatment-seeking or had parental concern for anxiety, and had clinical diagnoses of generalized anxiety disorder (GAD), separation anxiety disorder (SAD), and/or social phobia based on rating scales and interviews in the present study. Children participated in the study by completing questionnaires about their fear and anxiety symptoms, and their primary caregivers participated by completing questionnaires and a semi-structured interview about their children's anxiety symptoms, in order to assess differences in specific anxiety symptoms endorsed, severity and types of specific fears, and comorbidity with other anxiety disorders and with other emotional and behavioral difficulties.

Results: Comparisons between children with AD and children with ASD on the Screen for Child Anxiety and Related Emotional Disorders (SCARED) showed similar types of anxiety symptoms, by both parent and child report. However, there were slight developmental delays in the types of most commonly reported anxiety symptoms by child self-report. On the Behavior Assessment Scale for Children (BASC) questionnaire, parents of children with comorbid ASD reported more severe problems of Attention and Adaptive Skills, whereas parents of children with AD reported more severe problems of Somatization. Comparisons between groups were also made on overall severity of fears on the Fear Survey Schedule-Revised (FSSC-R) and indicated similar overall fear severity scores, similar severity scores on fear subscales, and a similar proportion of children in each group who endorsed clinically significant levels of fears.

Conclusions: The findings of this study support an emerging body of research suggesting that clinically anxious children with ASD exhibit similar types of anxiety symptoms and fears as children with anxiety disorders, without developmental disabilities. It is likely that their difficulties related to having the core symptoms of ASD (i.e., social difficulties, language impairments, and perseverative behaviors) do not produce anxiety symptoms that are different from those of a subset of children who have GAD, SAD, and/or Social Phobia. Measurement, treatment, and phenomenological reasons for this are discussed.

128.78 78 Acceptability of Cognitive-Behavioral Therapy for Teens with Autism Spectrum Disorders. C. E. Pugliese*, S. W. White and R. Nevill, *Virginia Polytechnic Institute and State University*

Background: Cognitive-behavioral therapy (CBT) is the primary, non-medical treatment of choice for mood and anxiety disorders of childhood. As identification rates of autism spectrum disorders (ASD) have risen, so has interest in adapting CBT to treat this population (Attwood, 1994). Although the efficacy of CBT modified for youth with ASD is promising, to the authors' knowledge, no previous research has examined teenagers' satisfaction with the treatment (Reaven & Hepburn, 2003). Objectives: The primary purpose of the present study was to evaluate teenagers' satisfaction with a manual-based CBT program. Additionally, we explored self-report measures of change. Methods: Four adolescents (12-14 years; 2 boys) with confirmed ASD and anxiety disorder diagnoses received the treatment, which addressed anxiety and social skills deficits. Teenagers had high intellectual capacity (IQ: 105-135). Following each individual therapy session and at treatment completion, the teenagers and their parents completed blinded measures of satisfaction with the treatment. Youth completed self-report measures of anxiety, loneliness, and

depression. Results: The data indicate that the youth found the sessions helpful (range: 5.82-8.83, on 1-10 scale) and overall program satisfaction was quite high (range: 7-10). Individual, followed by group, therapy were the components rated as most helpful. Parents also rated the sessions as helpful (6.18-9.91) with program satisfaction equally high (8-10). Individual therapy, followed by between-session assignments, were rated as the most useful components by parents. On self-report measures of change, there was considerable variability. Despite confirmed anxiety disorders at the beginning of treatment and independent clinician-rated change following treatment, teens reported little difficulty with anxiety and minimal change following treatment on the MASC (March, 1999) self report measure of anxiety. Only two teens reported clinically significant change (RCI = 5.67, 2.72). Two teens showed elevated scores on the depression measure at baseline. Change in depression, and social and emotional loneliness was variable and generally nonsignificant. Conclusions: Overall, both youth and parents found treatment helpful and acceptable, although they differed in what components they found most helpful. Results of this pilot study have potentially important implications for outcome measurement in treatment studies of ASD. Despite clinically confirmed anxiety disorders and parent-reported change with anxiety, the youth reported minimal problems with anxiety and inconsistent change. Furthermore, there was variability in both the report and change of depression and loneliness. In summary, the teenagers found the CBT program to be helpful, but there are implications for reliance on self-report measures of change. High-functioning youth with ASD may have difficulty recognizing or reliably reporting their symptoms of anxiety, depression, or loneliness. It is recommended that self-report measures for screening, diagnosis, and change be supplemented with clinician, teacher and parent ratings. References Attwood, T. (2004). Cognitive behaviour therapy for children and adults with asperger's syndrome. Behaviour Change, 21, 147-161. March, J.S. (1999). Multidimensional Anxiety Scale for Children manual. North Tonawanda, NY: Multi-Health Systems. Reaven, J. & Hepburn, S. (2003). Cognitive-behavioral treatment of obsessive-compulsive disorder in a child with Asperger syndrome: A case report. Autism, 7, 145-164.

128.79 79 Implementation of Ontology Driven Data Integration in the National Database for Autism Research. L. Young*[1], S. W. Tu[2], L. Tennakoon[2], J. McNiece[1], D. Vismer[1], M. E. Martone[3], A. K. Das[2] and M. J. McAuliffe[1], (1)*National Institutes of Health*, (2)*Stanford University*, (3)*University of California, San Diego*

Background: An autism ontology should document all terms relevant to the disorder; all relationships between these terms and with terms in other fields; and various assumptions and constraints used in the definition of autism endophenotypes. A data integration system could then assign unique identifiers to the ontological terms such that the same set of unique identifiers could also be assigned to terms and data in multiple data sources.

Objectives: Searches for autism information can be enhanced using both ontological relationships and reasoning. Such searches would be linked to research data of many types (such as clinical assessments, genomics, and imaging) from many labs. Representation of endophenotype could be standardized in the ontology, as well. This will lead to endophenotype driven queries and data integration from an endophenotype catalog.

Methods: The implementation uses the University of California San Diego (UCSD) Biomedical Informatics Research Network (BIRN) system to integrate data from multiple sources. This system includes a data integration environment comprising ontology for semantic integration; a mapping of ontology to data sources; a means to expose data sources to its grid; and middleware to manage federated queries and data extraction.

A draft of an autism ontology has been composed by a group at Stanford whose approach is to use ontologies and data models for querying and reasoning about phenotype. Semantic Web standards and technologies are used to encode the ontology.

Results: A proof of concept is presented here. The United States National Institutes of Health (NIH) National Database for Autism Research (NDAR) has adopted the BIRN data integration environment and linked it to autism research data. An NDAR user can log into the system and navigate to a list of endophenotypes. Clicking on a phenotype sends a query to the system to return data for all individuals satisfying the rules defining the endophentoype. The use of global unique identifiers for the individuals allows the user to also discover additional data such as genomics and imaging.

Conclusions: Efforts such as these will lead to an understanding of the processes necessary to increase the size of study populations by combining data from multiple institutions. This will lead to larger data sets and an increased likelihood of finding correlations between endophenotype and genetic variants or between endophenotype and variations in medical images. The hope is that strong correlations may be found and subsequently used in the clinic to diagnose susceptibility to autism disorders. This approach would be a faster, less expensive step in detecting autism susceptibility, leading to earlier intervention.

This research was supported by the Intramural Research Program of the NIH, Center for Information Technology (LY, MJM) and NIMH, NINDS, NICHD, NIEHS, and NIDCD (JM, DV); NLM 1P41LM007885 (SWT, LT, AKD); and NINDS RO1NS058296, NCRR RR04050, and RR08605 (MEM).

128.80 80 Controlling for the Influence of Education Level on Fidelity of Implementation of Pivotal Response Treatment for Children with Autism. J. Randolph*, J. Stichter, K. Visovsky, C. Schmidt and T. Schultz, *University of Missouri*

Background: Pivotal Response Training (PRT) combines the research on task interspersal, direct reinforcement, and role of choice in a treatment for autism spectrum disorders. PRT, through its training of parents of children with ASD, has repeatedly demonstrated widespread effects on many behaviors associated with language and social interaction (Koegel & Koegel, 2006; Koegel, Bimbela, & Schreibman, 2004). Little is known about parental characteristics associated with successful outcomes, despite literature on parent training that indicates the influence of variables other than child characteristics, such as income and parent level of education, on training and the resulting child outcomes (Reyno & McGrath, 2005). Objectives: The primary aim of this research was to control for the influence of education level on caregiver implementation of PRT for 3 caregiver-child dyads. The specific research question was: Does limited caregiver education affect level of fidelity of implementation?. Secondary research aims included: 1) Does the caregivers' level of fidelity impact the child's social-communication and play behaviors?, and 2) Are there potential wider affects on adaptive behaviors that can be captured with the Vineland Adaptive Behavior Scale (VABS)? Methods: A concurrent multiple baseline design across participants for baseline, training, and follow-up phases was utilized. All three children (ages 3-7) had a medical diagnosis of autism spectrum disorder (ASD) or pervasive developmental disorder (PDD) confirmed on the ADI-R or ADOS. In the first dyad, the caregiver was the child's grandmother. She provided primary care for the child, and had a high school diploma with no additional college education. In the second dyad, the caregiver was the child's biological father. He had a high school diploma with no additional college education. In the third dyad, the caregiver was hired by the child's parents as a home care provider. She had a high school diploma and two years of college education. Results: Two of the three caregiver-child dyads benefited from the intervention. The caregivers were trained to implement PRT with fidelity, and maintained fidelity of implementation in follow-up sessions. The children in these dyads increased responsiveness and appropriate play engagement as determined through direct observation procedures. One of the three dyads, however, received limited benefit from the intervention. The caregiver was unable to meet the level of fidelity required for mastery of implementation during the training sessions, and instead demonstrated inconsistent implementation. Likewise, the child's responsiveness was inconsistent, however the child's amount of time engaged in appropriate play increased during training. During the intervention for this dyad, a family emergency resulted in a three-week break from training, during which time the child was placed back in the care of her biological mother. No significant difference was found between the pre and post intervention scores on the Vineland Adaptive Behavior Scales for any of the participants. Conclusions: Level of education may not be as critical a variable in training success for PRT, as other variables, such as consistency of training sessions, or other family dynamics.

128.81 81 A Multi-Type Model of Inhibitory Control: Evidence from Individuals with Autism Spectrum Disorder. S. E. Christ*, L. B. Brubaker and J. H. Miles, *University of Missouri*

Background: The social and communicative challenges faced by individuals with autism spectrum disorder (ASD) are often compounded by additional difficulties with executive function. It remains unclear, however, to what the extent individuals with ASD experienced difficulties in inhibitory control. A multi-type model of IC suggests that IC may best conceptualized as

comprising at least three distinct subtypes: prepotent response inhibition, resistance to distracter interference, and resistance to proactive interference (Friedman & Miyake, 2004). To date, however, previous studies have focused on only one or two of these subtypes when evaluating the integrity of IC in individuals with ASD.
Objectives: To assess all three subtypes of IC within a single ASD sample thus providing new insight into the unique ASD-related pattern of sparing and impairment observed across different aspects of IC.
Methods: Thirty-seven individuals with ASD (mean age = 15.1 years) and an age- and gender-matched comparison group of thirty-seven neurologically uncompromised individuals (mean age = 15.1 years) participated. A counting Stroop task, a flanker visual filtering task, and a modified Brown-Peterson task were used to evaluate prepotent response inhibition, resistance to distracter interference, and resistance to proactive interference, respectively.
Results: After accounting for individual differences in non-inhibitory related abilities (e.g., processing speed) and overall level of functioning (IQ), there was no evidence of group-related differences in performance on the Stroop and Brown-Peterson tasks ($p > .05$ in all instances). ASD-related impairments were evident, however, on the flanker visual filtering task [$F(1, 72) = 7.464$, $p < .05$].
Conclusions: Taken together, the present findings suggest that ASD is associated with impairments in some, but not all, aspects of IC. Individuals with ASD appear to have difficulty ignoring distracting visual information, but prepotent response inhibition and resistance to proactive interference are relatively intact. The current findings also provide support for a multi-type model of IC.

128.82 82 Group CBT for Mood and Anxiety Problems in Adults with Asperger Syndrome: a Case Series. J. A. Weiss*[1] and Y. Lunsky[2], (1)*Centre for Addiction and Mental Health & York University*, (2)*Centre for Addiction and Mental Health*

Background: Individuals with Asperger syndrome (AS) are at increased risk for mental health problems compared to the general population, especially with regard to mood and anxiety disorders. Generic mental health services are ill-equipped to offer psychotherapeutic treatments to this population, and specialized supports are difficult to find. Few treatments for mood and anxiety disorders in adults with AS have been published. Objectives: This pilot study examines the effectiveness of a manual-based group cognitive behaviour therapy program (Mind Over Mood; Greenberger & Padesky, 1995) for use with adults with AS, and suggests ways to adapt the treatment to better suit the needs and abilities of this population.
Methods: Three adults (2 males and 1 female, 39 – 55 years of age) participated in 12 weeks of group CBT, provided by two psychologists (JW & YL). Approximately 4-6 weeks prior to the first session (baseline), each participant met with the researchers and completed the Beck Depression Inventory-II (BDI), Beck Anxiety Inventory (BAI), Adult Asperger Assessment (AAA; including the AQ and EQ; Baron-Cohen, Wheelwright, Robinson, & Woodbury-Smith, 2005), Structured Clinical Interview of DSM Disorders (SCID), and Weschler Abbreviated Scales of Intelligence – Short Form. At baseline, participants had clinically significant levels of depression or anxiety, and met DSM-IV criteria for a Past or Current Major Depressive Disorder, as well as various comorbidities (e.g., Panic Disorder, Post Traumatic Stress Disorder, etc…). All participants had Full Scale IQ estimates in the Average to Above Average range, and met criteria for Asperger Syndrome using the AAA. At the beginning of treatment, participants purchased a copy of Mind Over Mood, which was used as the basis for the intervention. Each week, participants completed the BDI and BAI prior to the session, which will also be completed at 8-weeks follow-up (study ongoing at time of abstract submission). Group feedback occured at the end of the study.
Results: This poster will present a case series tracking the progress made by each participant. Although emotional change as measured by the BDI and BAI was variable, all participants found the group helpful. Positive feedback included that participants did not feel as helpless with their problems and felt less anxiety than before, understood their moods, and were prepared to seek out individual counselling using a CBT framework. Participants remarked that using action plans were very helpful in solving day-to-day problems, and that the thought record was a useful way of examining automatic thoughts. There were also specific suggestions as to how group CBT can be improved for clients with AS.
Conclusions: There is evidence that CBT can be a useful mode of intervention for helping adults with AS with regard to problems with mood. Further research is needed to develop tailored group therapy programs that capitalize on the strengths

of individuals with AS, and support their difficulties.

128.83 83 Crises in Adolescents and Adults with Autism Spectrum Disorder. C. A. McMorris*[1], Y. Lunsky[2], C. Jaskulski[2], M. Viecili[2] and A. Khodaverdian[2], (1)*York University, Toronto*, (2)*Centre for Addiction and Mental Health*

Background: A crisis is defined as *an acute disturbance of thought, mood, behavior, or social relationship that requires immediate attention as defined by the individual, family or community* (Allen, Forster, Zealberg & Currier, 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, Clare, Holland & Kearns, 2006; Allen et al., 2008), loss of residential placements, serious injury, and admission to psychiatric facilities (Hardan & Sahl, 1999; Puddicombe & Lunsky, 2007). Despite the known negative impacts of crisis, limited research exists examining the occurrence of behavioural and other types of crises, as well as the severity and antecedents leading to crises in individuals with ASD.

Objectives: The present study aims to further examine the types and severity of crises occurring in individuals with ASD, as well as what events or factors contribute to crisis.

Methods: Thirty-three agencies from central and southeastern Ontario, who provide services (i.e., residential, day programs or case management) for adolescents and adults with Development Disabilities (DD; those individuals with intellectual disabilities and/or autism spectrum disorders), participated in this study. When a crisis occurred, staff were required to complete a Client Background Form (e.g., age, date, ethnic background, diagnosis, medication, etc.) and a Crisis Description Form (e.g., date of critical incident, description of critical incident, description of what led up to the event, etc.).

Results: Preliminary frequency analysis of the incidence of crises reported by agencies indicated a total of 1866 crises in individuals with DD, 33% (622) of which were experienced by individuals with ASD. Of these individuals with ASD (*M* = 30.9 years; 76.2% males), 19% had encountered multiple crises. The most common types of crises in the ASD group were: 1), Physical threat (27.5%); 2) Injury to others (25.9%); and 3) Property damage (21.2%). For those crises in the ASD group that were acts of aggression, staff rated the majority (36.6%) as *very serious*, that is, physical aggression without tissue damage, such as hitting, kicking and biting. Frequency of other types of crises, such as suicidal threat and AWOL (away without leave), will also be reported. Additionally, in order to examine the antecedents to the crisis in individuals with ASD, qualitative and frequency analysis will be conducted on staff descriptions of the event that led up to the crisis. Data collection is ongoing.

Conclusions: Overall, preliminary analysis suggest that individuals with ASD experience a variety of verbal and behavioral crisis, ranging from moderate to high severity. Further insight into this topic will contribute to our understanding of crises experienced by individuals with ASD. In addition, it may also help to inform the development of appropriate, crisis-specific supports for individuals with ASD, education and training for parents and professionals, and crisis prevention and intervention programs.

128.84 84 Teaching Emotion Regulation to Young Children with High Functioning Autism: An Intervention Study. N. M. Reyes* and A. Scarpa, *Virginia Tech*

Background: Previous research has found that children with Autism Spectrum Disorders (ASD) have pronounced deficits managing their emotions. Previous research has also shown that Cognitive Behavioral therapy improved symptoms related to anxiety and anger outbursts (Sofronoff et al., 2005, 2006). Researchers have found that parental confidence increases when parents are involved in the treatment process and become interventionist themselves (Schreibman, & Koegel, 2005). However, a CBT intervention for anxiety/anger in young children with ASD has never been tested.

Objectives: A group therapy intervention was implemented in order to examine: (i) whether children with ASD can improve regulation of their anger/anxiety related emotions, and (ii) whether parent's reported confidence in themselves and their child increases after their intervention.

Methods: Data were collected from eleven 5-7 year-old children (2 girls, 9 boys) with high functioning autism (HFA) and their parents. The Autism Diagnostic Observation Schedule was

administered to confirm children's diagnosis. Participants were randomly assigned to either an experimental or delayed-treatment control group. Group therapy intervention consisted of 9 concurrent child and parent sessions. During the sessions, children were taught to recognize anger and anxiety and to use strategies to manage those emotions. Parents reviewed the child sessions via a monitor and learned how to implement the strategies for use in other settings. Parent's perception of confidence in themselves and their child to manage their child's anger/anxiety related emotions were rated on a scale of 1 through 10 (1=not very confident; 10=very confident). Child emotion regulation skills were assessed using (i) a *Behavioral Monitoring Sheet in* which parents reported the frequency of anger/anxiety outbursts in one week, and (ii) the *Emotion Regulation Checklist*.

Results: Parents in the experimental group reported that children showed greater emotion regulation (i.e., fewer number of outbursts) than the delayed treatment group, $t(9)=1$, $p<0.05$. Parents also reported higher levels of emotion regulation abilities on the Behavioral Monitoring Sheet after treatment in both groups, $t(9)=12.51$, $p<0.05$. Parents, in the delayed treatment group, also reported higher levels of emotion regulation abilities on the Emotion Regulation Checklist in their children after treatment, $t(5)=-3.36$, $p<0.05$. Parental confidence in managing children's emotions increased in the experimental group for anxiety, $t(4)=-3.54$, $p<05$, and the delayed-treatment group for anger, $t(5)=-6.71$, $p<05$. Also, parent's perception of their child's confidence in regulating his/her anxiety increased in both the experimental, $t(4)=-4$, $p<0.05$, and the delayed-treatment group, $t(5)=-2.77$, $p<0.05$.

Conclusions: This study implemented a cognitive behavioral intervention to teach emotion management to young children with HFA. It was found that emotion regulation in the children improved after treatment. Additionally, including parents in the intervention appeared to increase parental self-confidence, as well as their confidence in their child to deal with emotional outbursts. In conclusion, cognitive behavioral intervention appears to be a promising tool for improving emotional regulation abilities in young children with HFA.

128.85 85 Use of a Picture Schedule to Prepare Children with ASD for Participation in a Research Study. H. Austin*[1], K. Kaparich[1], S. Hepburn[2] and A. Reynolds[1], (1)*University of Colorado Denver*, (2)*University of Colorado Denver School of Medicine*

Background: Autism Spectrum Disorders (ASD) are characterized by a need for routine and predictability. Individuals with autism often have great difficulty with transitions and novel situations. The resulting anxiety can cause significant stress and lead to maladaptive behavioral responses. In addition to teaching appropriate behaviors, Social Stories (Gray 1994, 2000) have been used to increase participation in new routines. Picture schedules have been similarly effective in helping ASD children adjust to changes in routine (McClannahan and Krantz, 1999; Dettmer et al., 2000) and to be prepared for novel events (Ivey et al., 2004).

Objectives: We investigated the usefulness of a picture schedule to prepare children with autism for participation in a research study on intestinal permeability.

Methods: Parents of children with autism (n=51; diagnoses confirmed by ADOS and SCQ) and parents of children with a history of typical development (n=26) participating in a study of intestinal permeability were sent a picture schedule illustrating the procedures involved in the research study. Medical procedures included drinking a sugar solution, 6 hour urine collection, and a blood draw. Parents were instructed to review the picture schedule with their child prior to the appointment. At the end of the study, parents were asked to complete a five question survey about their satisfaction with the picture schedule.

Results: Forty-eight (63%) families completed the survey on the use of the picture schedule. Twenty-six out of 30 with ASD (87%) and 14 out of 18 with typical development (77%) reported using the picture schedule. Of those that responded, 96% of the parents of children with ASD and 100% of the parents of typically-developing children rated the picture schedule as either "Somewhat Helpful" or "Very Helpful". Child report was also solicited through the parents, and of the 17 families who recorded an answer for their child, 82% of the participants with ASD felt that the picture schedule was either "Somewhat Helpful" or "Very Helpful". One

hundred percent of the typically developing subjects responded that it was either "Somewhat Helpful" or "Very Helpful". One hundred percent of parents from both groups said that they would recommend picture schedules to other families preparing their child for a visit to the hospital.

Conclusions: Our study suggests that picture schedules illustrating medical procedures are acceptable to families and may be helpful for both research and clinical projects. Future studies employing random assignment to groups (e.g., with and without pictures) and using more rigorous measures of feasibility, acceptability, child anxiety and parent stress would be a very good next step. Researchers may want to consider routinely incorporating picture schedules into their protocols to reduce the stress children experience when participating in a study.

128.86 86 Treating Anxiety Disorders in Adolescents with High Functioning Autism: The Case of John. A. Drahota*[1] and J. J. Wood[2], (1)*University of California, San Diego*, (2)*University of California, Los Angeles*

Background: Adolescents with high functioning autism (HFA) are at heightened risk for anxiety disorders (Bellini, 2004), which can interfere with adaptive functioning in academic, family, and social settings. Literature suggests that excessive anxiety is associated with adolescents' increased negative thoughts, behavioral problems, and adaptive functioning (Farrugia & Hudson, 2006). Given the pervasive nature of HFA, the additional negative impact of anxiety disorders may make worse the difficulties experienced by these adolescents. While emergent literature involving randomized, controlled trials provides empirical support for cognitive behavioral treatment of anxiety disorders in *children* with HFA (Chalfant et al., 2007; Wood et al., in press), adolescents with HFA have been largely ignored in the treatment literature despite their clinical need.

Objectives: Accordingly, this presentation provides a brief history of the Family Cognitive Behavioral Therapy (FCBT) manual, *Building Confidence* (Wood et al., 2007). Moreover, research-based modifications and enhancements to the treatment manual, including their scientific rationale, will be examined. The presentation will conclude with a case study involving John, a 13-year-old male with HFA and comorbid generalized anxiety disorder (GAD), for which the GAD caused significant distress and disruption in his and his family's life and interfered with John's academic performance and daily living skills.

Methods: A comprehensive assessment battery was administered at pretreatment, posttreatment, and 1-year posttreatment by a diagnostician unaware whether John received treatment. The assessment battery included the Anxiety Disorders Interview Scale for *DSM-IV*: Parent and Child versions (Silverman & Albano, 1996), a semi-structured interview yielding reliable diagnoses of anxiety disorders. In addition, John's mother completed several paper-and-pencil measures, including the parent version of the Multidimensional Anxiety Scale for Children (March, 1998), a 39-item measure of anxiety with robust reliability and validity (Wood et al., 2002), the Child Anxiety Interference Scale (Langley et al., 2004), a 34-item scale assessing children's functional impairment in school, social, and home situations due to anxiety, and the Social Skills Rating System (Gresham & Elliott, 1990), consisting of 55 items assessing social skills and competing problem behaviors.

Results: After 16 weeks of the modified FCBT, involving both John and his mother, symptoms of GAD were ameliorated and the clinical severity of the GAD was reduced to a nonclinical level. Further, significant improvements in his adaptive functioning, such as daily living and social skills, academic performance, and family cohesion, were reported at posttreatment and gains were maintained over a 1-year period. Feasibility and fidelity to treatment strategies were found to be quite good.

Conclusions: Despite developmental shifts from childhood to adolescence, which may impact the feasibility and fidelity of family cognitive behavioral therapy, modified and enhanced FCBT may be an appropriate treatment for adolescents with HFA and comorbid anxiety disorders, leading to improved overall adaptive functioning.

128.87 87 The Rostrum Is Smaller in High Functioning Adolescents with Autism Spectrum Disorders and Associated with Subclinical Autistic Traits in Typically Developing Adolescents. N. A. Dankner*, M. Reddish, A. Martin, J. N. Giedd and G. L. Wallace, *National Institute of Mental Health, National Institutes of Health*

Background: Autism spectrum disorders (ASDs) are associated with abnormal corpus callosum morphology. However, (1) previous investigations of subregional callosal morphology in ASD provide

inconsistent results, and (2) it remains unknown if, extending this line of inquiry beyond the ASD diagnosis, corpus callosum morphology is associated with subclinical autistic behavior.

Objectives: The present study examined corpus callosum morphology in adolescents with high functioning ASDs versus typically developing adolescents and its relationship with subclinical autistic traits.
Methods: T1-weighted MP-RAGE MRI volumes were acquired at 3T from 30 adolescents (87% male), each diagnosed with a high functioning ASD and from 30 typically developing adolescents (90% male) matched group-wise on age (range=12-24) and IQ (>85). ASD diagnoses (i.e., high functioning autism, Asperger's syndrome, pervasive developmental disorder-not otherwise specified) were based upon DSM-IV criteria as well as scores from the Autism Diagnostic Interview and the Autism Diagnostic Observation Schedule. The most medial saggital slice was used to measure the area of the corpus callosum. Witelson's method, providing metrics of seven subregions of the corpus callosum (the rostrum, genu, rostral body, anterior midbody, posterior midbody, isthmus, and splenium) was used. Subclinical autistic traits were acquired through parent ratings from the Social Responsiveness Scale.

Results: Overall corpus callosum area was not different between groups; however, one subregion, the rostrum, was found to be smaller among adolescents with ASD. Furthermore, among typically developing adolescents, parent ratings of subclinical autistic traits were negatively correlated with rostral area (uniquely among the seven corpus callosum subregions) such that higher autistic trait ratings were associated with smaller rostral area.
Conclusions: Smaller than average rostral area in adolescents with ASD may reflect abnormal connectivity in frontal (particularly ventral) regions. Furthermore, this relationship may extend beyond an ASD diagnosis since rostral area was also associated with subclinical autistic traits among typically developing adolescents.

128.88 88 Hemispheric Asymmetries in Neural Resource Allocation in Auditory Language Cortex in Children with Autism and Typically Developing Children: An MEG Investigation. N. M. Gage*, A. L. Isenberg, P. T. Fillmore, K. Osann and M. A. Spence, *University of California, Irvine*

Background: recent neuroimaging investigations of cortical activation patterns in individuals with autistic disorder (AD) have reported local overconnectivity in sensory cortices and related results to neural resource allocation abnormalities in AD. We used Magnetoencephalography (MEG) to investigate the time course of neural activation for speech and nonspeech sounds in typically developing (TD) children and children with AD.

Objectives: to determine if neural activation levels in auditory language cortex (i) were generally higher in children with AD as compared to TD controls; (ii) changed over time with repeated exposure to sounds, and (iii) differed as a function of cerebral hemisphere and stimulus class (tones vs. speech).

Methods: We used a 148 channel Magnes 2500 Whole Head Biomagnetometer System™ (4-D Neuroimaging, San Diego, CA) to record the auditory evoked M100 in 10 TD controls (8 boys, 10y 5mo (1.2)) and 11 children with AD (9 boys, M 11y 0mo (2.0). Stimuli: TONES – 250, 500, 1000, and 2000Hz sinusoids; SPEECH – 4 natural tokens of consonant-vowel syllables. Each stimulus was presented 100 times in an interleaved fashion. Recording consisted of two 4-5m scans of 400 epochs each. Each scan was divided into 4 equal blocks representing the first, second, third, and final 100 epochs and M100 amplitude (femtoTesla, fT)) was measured for each block, stimulus class, hemisphere, and child.

Results: TONES - Neural activation level (grand mean M100 amplitude), was lower in TD (114.0 (8.6). vs. children with AD (120.0fT(9.5)). SPEECH - Overall neural activation level was higher in TD (114.6 (9.5) vs. children with AD (104.0 (5.3). The timecourse of neural activation levels differed sharply for TD vs. children with AD for both TONES and SPEECH. TONES – for TD, M100 amplitude decreased (-17%) in LH (125.0(17.9) to 104.1(34.1)) and increased (+14%) in RH (105.1(11.0) to 120.0(19.1)) from the first to the final block. Children with AD showed the opposite effect, with M100 amplitude that slightly increased (+2%) in LH (108.8(8.7) to 110.5(21.3)) and slightly decreased -5% in RH (126.3(20.4) to 119.5(34.9)). SPEECH – for TD, M100 amplitude increased (+14%) in LH (108.3fT(10.5) to 123.1(12.2)) and increased (10%) in RH (103.9(6.1) to 112.6(10.4)). For children with AD, M100 amplitude decreased (-

7%) in LH (103.9(5.0) to 96.7(10.1)) and decreased (-5%) in RH (103.5(10.1) to 98.7(6.0)).

Conclusions: in TD children, we report dynamic hemispheric shifts in resource allocation as a function of time and stimulus class: a rightward shift in neural activation for tones and bilaterally-increasing neural activation for speech. Results provide new data regarding the temporal dynamics of neural resource allocation in sound processing in TD children, and are in good accord with previous neuroimaging reports of hemispheric biases in decoding spectral and temporal features in sounds. We report an opposite effect in children with AD, with a slight leftward shift for tones and bilaterally-decreasing activation for speech. Results provide new data regarding the temporal dynamics of neural resource allocation in sound processing in children with AD, and provide further evidence that neural mechanisms underlying sound processing are organized in a fundamentally different manner in this population.

128.89 89 Use of the Slicer3 Toolkit to Produce Regional Cortical Thickness Measurement of Pediatric MRI Data. H. C. Hazlett*[1], C. Vachet[2], C. Mathieu[2], M. Styner[2] and J. Piven[3], (1)*University of NC*, (2)*UNC*, (3)*University of North Carolina*

Background: The data analysis of neuroimaging data from pediatric populations presents several challenges. There are normal variations in brain shape from infancy to adulthood and normal developmental changes related to tissue maturation (i.e., myelination of white matter) that create problems in the direct application of tools designed for adult brain.

Objectives: Our team has created a computer processing tool to produce regional cortical thickness maps appropriate for pediatric MRI data, and is developing a similar pipeline to perform local cortical thickness measures. This application has been integrated into the Slicer3 toolkit. Slicer3 is a cross-platform application for analyzing and visualizing medical images. It is an open source application and is funded by a number of large-scale NIH supported efforts, including the National Alliance for Medical Image Computing (NA-MIC).

Methods: We have used a pediatric dataset containing 90 cases of 2-4 year olds with typical development, autism, and developmental delay. This data was input into our regional cortical thickness pipeline, which involves input from T1-weighted MRI data, and produces tissue segmentation, followed by regional atlas deformable registration, to compute a lobar cortical thickness for each case.

Results: Validation tests of this tool have been computed on a small dataset of 20 2-4 year old scans.

Conclusions: The Slicer3 toolkit provides an accessible and versatile platform to conduct image processing of pediatric MRI data, in this case, regional cortical thickness data.

128.90 90 Investigating Transverse Relaxation Time Abnormalities of White Matter in Autism. Y. Gagnon*[1], D. Drost[1] and R. Nicolson[2], (1)*University of Western Ontario*, (2)*The University of Western Ontario*

Background: Autism is a developmental disorder characterized by social deficits, impaired communication, and restricted and repetitive patterns of behavior. Although there is strong evidence that autism is associated with abnormal brain development, the anatomical extent and timing of these neurobiological differences are unknown. One method to examine tissue abnormalities in vivo is quantitative transverse relaxation time (T2) imaging. T2 is influenced by the molecular environment and tissue properties. We have reported an increase in overall white matter T2 in children and adolescents with autism, with a follow-up study finding disproportionally localized increases in the frontal and parietal lobes. This pattern of increased T2 parallels that of increased white matter volume of some volumetric studies in autism. A recent volumetric study has attempted to further localize volume increases in white matter by radially parcellating it into radiate and inner zones and appropriate subcompartments.
Objectives: The purpose of this study was to investigate T2 differences in patients with autism with a similar parcellation scheme to determine if the pattern of T2 abnormalities remained similar to that of volumetric studies.

Methods: Twenty-one male patients with autism between the ages of 6 and 16 and 20 male controls in the same age range participated in this study. The diagnosis was made according to DSM-IV-TR criteria using the Autism Diagnostic Interview-Revised, the Autism Diagnostic Observation Schedule. All patients had non-verbal IQ greater than 70. Control subjects were drawn

from the local community and were assessed to rule out any psychiatric disorders. The groups did not differ significantly in age, sex, race, full-scale IQ, or non-verbal intelligence. Ten patients were medication-naïve at the time of their scan, while 3 others had discontinued their medication prior to the scan. 16 patients required sedation with oral midazolam in order to complete the scan. T2 data were acquired on a 3T magnetic resonance scanner using a Gradient Echo Sampling of the Free Induction Decay and Echo (GESFIDE) sequence. T2 maps were reconstructed for each subject. Spatial normalization was performed using SPM5 using an adult T2 template as a target. Masks for each region of interest (superficial white matter, radiate white matter and deep/bridging white matter) in standard space were generated using the Pickatlas toolbox for Matlab and the DTI-81 white matter atlas. Mean T2 values for each region of interest were then calculated by multiplying the normalized T2 maps by these binary masks.
Group differences in white matter T2 were investigated using a Repeated-Measures Analysis of Covariance. Given the changes in T2 described in childhood, we covaried the statistical analysis of T2 for age.

Results: In a preliminary analysis, a repeated measures ANCOVA revealed no significant main effect or interactions involving diagnosis, though the main effect for diagnosis approached significance level ($p<0.08$).

Conclusions: Patients in this study did not show an increase in superficial or radiate white matter T2 paralleling that of volumetric studies. Further work will focus on optimizing and validating image registration and parcellation techniques used in the analysis.

128.91 91 Immediate Social Context in Face Processing: An ERP Study of Autism. S. Shultz*[1], W. Jones[2], A. Klin[2] and J. McPartland[1], (1)*Yale University*, (2)*Yale University School of Medicine*

Background: Previous research has shown that individuals with autism fail to attribute social meaning to ambiguous visual stimuli, resulting in maladaptive mental representations of the social environment. In contrast, typical individuals, but not individuals with autism, show enhanced face-related electrophysiological brain activity (N170) when viewing ambiguous stimuli subsequent to viewing face-relevant contextual cues. In typical viewers, face-sensitive areas of the fusiform gyrus also activate in the absence of intrinsic facial features when a face is implied by the context of a human form. Previous research has not yet addressed whether individuals with autism imbue ambiguous stimuli with social meaning in this type of immediate social context.

Objectives: To investigate the N170 as an electrophysiological index of imputation of social meaning in autism.

Methods: Continuous ERP data were recorded while adolescents with autism (n=15) and typical controls (n=15) viewed images of degraded faces with a human body, degraded faces alone, bodies alone, clear faces alone, and clear faces on bodies.

Results: Analyses replicated findings of increased N170 amplitude to ambiguous stimuli subsequent to viewing face-related contextual cues in typical individuals but not in individuals with autism. Analyses in progress will examine between-group differences in enhanced N170 to ambiguous stimuli presented within an immediate social context.

Conclusions: Determining whether face-specific N170 responses can be elicited by immediate contextual cues will provide insight into the clinical problem in autism of failing to interpret ambiguous stimuli in socially meaningful ways, a critical ability for optimizing adaptive responses to the surrounding social environment. Investigating this failure will offer insight into the mechanisms of social brain dysfunction in autism, an objective critical for effective intervention and early detection.

128.92 92 Ratings of Facial Attractiveness by High-Functioning Individuals with Autism. C. A. Best*[1], D. Wilkinson[1], M. S. Strauss[1] and N. J. Minshew[2], (1)*University of Pittsburgh*, (2)*University of Pittsburgh School of Medicine*

Background: Although differences in face perception abilities have been widely studied by autism researchers, there is limited research on whether individuals with autism perceive facial attractiveness as typically developing individuals do. White, Hill, Winston, and Frith (2008) found that adults with Asperger Syndrome were less accurate than matched control adults at judging facial attractiveness, especially if the stimuli were the same sex as the participant. Yet researchers have not considered whether difficulty judging

facial attractiveness extends to individuals diagnosed with autism.

Objectives: The aim was to determine if there are differences in the perception of facial attractiveness in high-functioning individuals with autism versus typically developing individuals.

Methods: Participants with autism were high-functioning adults (18 – 45 years). Participants without autism were matched to the autism group on age, gender, verbal, performance, and full scale IQ. Sixty color face stimuli were presented individually on a screen with equal numbers of male and female faces. Participants were asked to rate the attractiveness of each face on a 7 point scale. Face stimuli were previously rated by an independent group of raters (i.e., a class of undergraduate students). Stimuli were selected based on the class ratings so as to present an equal range of attractive, average, and unattractive faces.

Results: Analyses revealed that mean attractiveness ratings by the autism group and control group were correlated with the class ratings of attractiveness. However, results indicated that whereas the control group was highly correlated with the class, the autism group was only moderately correlated with the class. Additional analyses of the highest and lowest rated faces indicated that the moderate correlation between the class and the autism group was driven only by their agreement for the unattractive faces. There was much less agreement for average and attractive faces between the autism group and the class ratings compared to the control group.

Conclusions: Attractiveness ratings by the control group were highly correlated with the ratings by the class reflecting agreement for perception of attractive versus average versus unattractive faces. In contrast, attractiveness ratings by the autism group were only moderately correlated with the ratings by the class largely due to agreement for judging unattractive faces. Unlike the control group, the autism group did not appear to distinguish attractive from average faces. Given that perception of facial attractiveness emerges early in development as evidenced by typically developing 2-month-old infants' preference to look at attractive versus unattractive faces (Langlois, et al. 1987), it is remarkable that adults with autism have even some difficulty judging attractiveness. Prior research has demonstrated that perception of facial attractiveness is driven primarily by facial feature typicality (e.g., Rubenstein and Langlois, 2002). Faces with average or typical features are considered attractive, and faces with atypical or distinctive features are considered unattractive. The current results suggest that, perhaps, individuals with autism never abstract a representation of how faces vary with respect to typicality, which could explain why they easily judge faces as unattractive, but have more difficulty judging faces as attractive or average.

128.93 93 Affect Recognition Skills across Four Nonverbal Channels in Children with Autism-Spectrum Disorders and Their Typically-Developing Peers. N. M. Russo*, C. McKown and M. Lipton, *Rush University Medical Center*

Background: We currently have an incomplete understanding of the social-emotional processing impairments that give rise to social disability among children with autism-spectrum disorders (ASDs). Affect recognition, or the ability to infer others' emotions from nonverbal cues, is an important contributor to social success and has been proposed as one of the deficits in ASD. Most studies have examined children's ability to infer emotions from photographs of facial expressions. Although some studies find that children with ASDs have impaired affect recognition skills, other studies find no differences between children with ASDs and their typically-developing peers.**Objectives:** The objective of this study is to compare the ability of children with ASDs to recognize others' emotions from four nonverbal channels (facial expression, tone of voice, posture, and gait) to that of their typically-developing peers. We hypothesize that averaged across nonverbal behavioral channels (faces, voices, posture, and gait), compared to their typically-developing peers, children with ASDs will have difficulty inferring others' emotions. **Methods:** A total of 160 typically-developing children and 20 children with ASDs (ages 5 to 14 years) completed multiple tests of affect

recognition, spanning four nonverbal channels. Using a regression analysis of the typically-developing sample, we estimated expected means at each age and the expected variability around those regression estimates. The degree of deviation (SD) from that expected mean was calculated for each child with an ASD. **Results:** Children with ASDs consistently score lower on affect recognition measures skills than their typically-developing age-mates. **Conclusions:** The data provide a clear and consistent picture that compared to a large sample of typically-developing children, children with ASDs have mild to moderate nonverbal accuracy deficits across a range of nonverbal behaviors. These data add to our understanding of social-emotional processing impairments. Future studies may investigate the application of this information to the development of new assessment and treatment measures.

128.94 94 What's in the Face? the Comprehension of Facial Expressions in Sign Language by Deaf Children with Autism. T. A. Denmark*, J. Swettenham, J. Atkinson and R. Campbell, *University College London*

Background:

Children with autism tend to look less at others' faces (Klin, Jones et al., 2002; Dawson et al, 2004, 2005) and show deficits on a range of face processing tasks compared to their peers (Schultz 2005). Such impairments might have specific consequences for deaf children with autism who use sign language, as the face plays an important role in sign language, communicating *both* linguistic as well as affective information. This is the first known study to date which examines the extent to which deaf children with autism comprehend the *linguistic* use of the face in sign language.

Objectives:

Are deaf individuals with autism impaired at *comprehending* a facial act that has linguistic significance in British Sign Language (BSL): the negation of a statement?

Methods: **Test of negation comprehension in BSL**

Sentences which use negation involve expressing that something is not present or in existence (Sutton Spence and Woll 1999, chapter 4). Negation in BSL is unique in that its linguistic meaning can be conveyed through *face actions alone*, or through a combination of the lexical sign for negation *(hands), as well as the face*. In our task deaf children with autism and typically developing deaf children (controls) watched short video clips of a signer producing signed phrases in three conditions; i) positive (27 trials), ii) negative: *hand sign and facial action* (16 trials), and iii) negative: *facial action alone* (16 trials). After each trial the child is shown two pictures and asked to choose the picture which matches the sign.

It is hypothesised that deaf children with autism will have greater difficulty relative to controls at comprehending negation in the face only condition compared with the face and hands condition. The controls are expected to show no difference between comprehension of negation in both face and hands and facial action only conditions.

Results:

Results from typically developing deaf children indicate that there is no significant difference in accuracy between the two negation conditions (face and hands and facial action alone). Preliminary results from the deaf children with autism suggest that they do show some difficulty comprehending negation when it is on the face alone compared with when it is on the face and hands.

Conclusions:

Results suggest that deaf children with autism may have some difficulties comprehending facial expressions in sign language compared to their typically developing peers. These findings indicate that it is possible for face processing difficulties associated with autism to have subtle effects on sign language comprehension.

128.95 95 Defining Category Abilities and Challenges in Adolescents with Autism VS. Those with Optimal Outcomes. L. Naigles*, M. Helt, M. Rosenthal, E. Troyb, K. Tyson, I. M. Eigsti and D. Fein, *University of Connecticut*

Background:

Many children with autism spectrum disorder (ASD) acquire a sizeable lexicon; however, they may understand and/or store the meanings of words differently from typically developing children (Gastgeb et al., 2006; Kelley et al., 2006; Rapin & Dunn, 2003). In particular, Kelley et al., (2006) found continuing difficulties with categorical induction, which involves realizing

when properties associated with object A should also be associated with object B—such as when A and B have the same labels—in children originally diagnosed with autism who by the age of 7 years had achieved an optimal outcome.

Objectives:

We assess category induction abilities in more depth, comparing the optimal outcome children when they reached adolescence with mental age-matched typically developing children and high-functioning children with autism.

Methods:

Three groups of young adolescents are being tested: typically developing (TD, n = 18, *M*(age) = 13.4 years), high-functioning with autism (HFA, n = 6, *M*(age) = 12.8 years), and optimal outcome (OO, n = 11, *M*(age) = 13.0 years). The children were matched on their WASI scores (*M*(TD) = 116.39, *M*(HFA) = 115.83, *M*(OO) = 116.73), and scored at age level or above on the PPVT (*M*(TD) = 122.11, *M*(HFA) = 105.32, *M*(OO) = 113.73). All children were given a categorical induction task adapted from Guthiel and Gelman (1997). Children were shown two sets of pictures. Set A included five identical animals in different positions (e.g., five yellow snakes) or a single animal (e.g., one yellow snake); set B included five animals of the same kind but of different appearance (e.g., five snakes of varying colors and patterns, none yellow). Different properties were assigned to the animals of set A (e.g., blue eyes) vs. set B (e.g., gray eyes). For the test trial, an entirely new animal of the same kind was presented (e.g., a new snake), and the children were asked whether this animal was likely to have the same property as those in set B or those in set A. Guthiel and Gelman reported that typically developing adults, and children as young as 9 years of age, consistently extended the property belonging to the more diverse set (e.g., B) to the new animal.

Results:

All groups performed similarly with control questions (comparing single vs. identical sets), showing they understood the task. The TD children consistently extended the property belonging to the more diverse set (*M* = 4.67 out of 6, *SD* = .91), as did the OO children (*M* = 4.45, *SD* = .82). In contrast, the HFA children were more likely to extend the property belonging to the homogeneous or single sets (*M* = 3.67, *SD* = 1.03). Both TD and OO children performed significantly better than HFA children ($t(22) = 2.26$, $p < .05$ and $t(15) = 1.73$, $p = .05$, respectively).

Conclusions:

These OO children seem to have overcome their earlier difficulties with categorical induction as they extended properties much like the TD children. In contrast, such category difficulties are still evident in high-functioning adolescents who carry the autism diagnosis.

128.96 96 Effects of Face Training and Intervention on Face Memory in Young Children with Autism Spectrum Disorders. K. M. Venema*[1], L. Xuereb[1], E. J. H. Jones[1], D. Kamara[1], K. Merkle[1], S. Faja[1], G. Dawson[2] and S. J. Webb[1], (1)*University of Washington*, (2)*Autism Speaks, UNC Chapel Hill*

Background: Processing information from faces is thought to be central to many of the social and communicative skills that are impaired in Autism Spectrum Disorder. Improving face recognition skills may thus be an important target for early intervention. However, little is known about the effects of intervention on face recognition in young children with ASD.

Objectives: To examine the effect of an intensive randomized intervention, which included a face training component, on the performance of toddlers with ASD during a face recognition test.

Methods: Three groups of children were included: toddlers with general developmental delays (DD group), toddlers with an ASD who participated in community intervention programs (ASD-C group), and toddlers with an ASD who participated in the *University of Washington Denver STAART* model of intervention (ASD-UW group). UW intervention (Smith, Rogers & Dawson, 2008) was a two year early intensive behavioral therapy that also included training on face recognition using an individualized photo book containing pictures of the child's parents, family members, and therapists amongst a number of distracters.

The face recognition test was administered when children were 24- to 60-months. Children were asked to 'point to mom' from a set of six pictures. Children were tested with both full faces and inner features only.

Results: Preliminary results indicate that the

mean difference in scores on the face recognition test between the DD, ASD-C and ASD-UW groups did not significantly differ. However, 26 of 48 children tested to date scored 100% on the task. Notably, thirteen subjects from the ASD-UW group (68%) were able to successfully complete the entire task compared with only four toddlers in the ASD-C group (31%).
Conclusions: Children in the DD, ASD-C and ASD-UW groups performed similarly on the face recognition task, although a ceiling effect may have masked any underlying trends. However, the children in the ASD-UW group were more likely to complete the test than those in the ASD-C group, suggesting that intensive intervention including training on facial picture identification might facilitate compliance during a testing situation. Further analysis will include an analysis of the errors children made during picture selection, which may provide insight into the face recognition strategies used by children who did not score full marks on the test.

128.98 98 Planning and Prospective Memory Performance in Autism Spectrum Disorders: Comparisons Between Laboratory-Based Performance and Performance in Everyday Life. M. Altgassen*, M. Schmitz-Hübsch and M. Kliegel, *Technische Universitaet Dresden*

Background:

Individuals with autism spectrum disorders (ASD) often show difficulties to organize and coordinate everyday activities. They are impaired in time management, preparation and sequencing of actions. These deficits with planning ahead have been found in time-based prospective memory tasks (PM; Altgassen et al., in press) and multi-tasking paradigms (Mackinlay et al., 2006) in the laboratory.

Objectives:

The present study compared laboratory-based PM performance with everyday performance in individuals with ASD.

Methods:

Nineteen children with high-functioning ASD and 19 age- and ability-matched neurotypical controls completed an event-based PM task that was embedded in a visuo-spatial working memory task. Everyday planning performance was assessed with proxy ratings (DEX-Questionnaire, Prospective and Retrospective Memory Questionnaire).

Results:

Analyses of variance (ANOVAs) indicated no group differences in the event-based PM task ($F(1,36)=.55$, $p>.05$). However, regarding ratings of everyday performance significant group effects were revealed with the ASD group being rated as showing poorer performance in both measures (DEX: $F(1, 36)=43.89$, $p < .001$; PRMQ: $F(1,36)=15.58$, $p<.001$). Correlational analyses indicated relations between laboratory-based and everyday performance (DEX $r=-.36$, $p<.01$; PRMQ $r=-28$, $p<.05$).

Conclusions:

Individuals with ASD showed spared performance in a laboratory-based event-based PM task. This is in contrast to proxies' ratings of everyday difficulties with planning tasks in participants with ASD and previous research on laboratory-based time-based PM performance (Altgassen et al., in press). Everyday PM tasks and time-based PM tasks are less structured than event-based PM tasks and demand more self-initiated processing which may underlie the here reported ASD deficit. Importantly, ratings of everyday performance and laboratory-based performance were related, thus, indicating that generally poorer laboratory-based performance was associated with more deficits in daily life.

128.99 99 Visual Search in Static and Dynamic Self-Motion Environments: An Eye-Tracking Study. E. Sheppard*, D. Ropar, G. Underwood and E. Van Loon, *University of Nottingham*

Background: Research has shown that those with ASD excel on visual search tasks that require them to find a target stimulus within a figure or array of objects (e.g. Shah and Frith, 1983, O'Riordan et al., 2001). These findings can be explained by various theories of perceptual processing in ASD including Enhanced Perceptual Functioning (Mottron & Burack, 2001), Weak Central Coherence (Frith, 1989), and superior systemising skills (Baron-Cohen, 2002). However, previous studies have only used static stimuli, so it is unclear whether superior visual search skills would be evident with moving stimuli. This is important as in everyday life we frequently need to search for objects within moving arrays, often whilst being in motion ourselves. Additionally, previous research has not explored visual search for targets embedded in social stimuli. It has been found that individuals with ASD tend not to orient

to social aspects of their environment (e.g. Klin et al., 2002), suggesting that they might find search for targets embedded within social stimuli more challenging.

Objectives:

This study aimed to explore the effects of motion and social relevance on visual search ability in participants with and without ASD. It was predicted that those with ASD would show superior visual search performance to comparison participants in both static and dynamic conditions. However, this advantage would disappear when searching for a target within a social stimulus.

Methods:

20 adult males with HFA or AS, and 40 matched comparison participants (20 male, 20 female) participated. They viewed 40 three-dimensional graphical animations of a driver's view of road scenes and 40 still images of similar scenes. The dynamic scenes contained simulated self-motion, as though the viewer was moving through the environment. Each scene contained a target shape (circle or triangle) hidden within the scene. In each condition (static and dynamic) the target was on a social stimulus (i.e. a person) 25% of the time, and on a non-social object (e.g. car, road, building) 75% of the time, roughly corresponding to the proportion of the screen covered by social and non-social stimuli respectively. Participants were instructed to respond with a key-press as soon as they located the hidden shape. They then identified verbally which shape was present and where it was within the scene. Accuracy and response time were recorded. Participants' eye movements were recorded using a tobii portable eye-tracker.

Results: Initial analyses suggest that whilst the groups did not differ in reaction time for either task (static or dynamic), participants with ASD were more accurate (i.e. correctly identified more targets) than male comparison participants on the static version of the task. Analysis of the eye movement data will also be presented.

Conclusions: Implications of the findings for theories of perceptual and social processing in ASD will be discussed.

128.100 100 Theory of Mind: The Importance of the Right Connections. S. J. Carrington*, M. Rushworth and A. Bailey, *University of Oxford*

Background: Evidence from post mortem and neuroimaging studies suggests that autism spectrum disorder (ASD) may be a disorder of connectivity (e.g. Bailey et al., 1998; Courchesne & Pierce, 2005; Just et al., 2004). The potential impact of disordered connectivity on cognitive function is yet to be fully established. In typically developing (TD) individuals, several brain regions have been associated with Theory of Mind (ToM), including the medial prefrontal cortex, temporoparietal junction, and superior temporal regions. It has been suggested that these distinct regions may comprise a ToM network. ToM is a core deficit of ASD (e.g. Baron-Cohen et al., 1985; Perner et al., 1991) and functional neuroimaging studies have indicated abnormal activity within (Happé et al., 1996; Baron-Cohen et al., 1999) and functional connectivity between (Castelli et al., 2002) areas typically associated with ToM. Furthermore, diffusion tensor imaging has revealed abnormalities in the connective white matter tissue between ToM regions in ASD (Barnea-Goraley et al., 2004).

Objectives: 1) to investigate the ToM network in TD individuals; 2) to determine whether disruption to connections between network components might contribute to the ToM deficit in ASD.

Methods: Behavioural and functional MRI data from eighteen males with ASD and eighteen TD males are reported. ToM was assessed using a comic strip paradigm based on the task devised by Sarfati et al. (1997). DTI data were acquired and tract-based spatial statistics conducted on measures of fractional anisotropy (FA) to assess white matter (WM) integrity.

Results: The pattern of activity evoked by ToM comics in TD individuals is largely consistent with results from previous studies. Moreover, the same comics evoked a different pattern of activity in individuals with ASD, particularly in medial prefrontal regions. Analysis of the diffusion data revealed several regions of altered white matter integrity (FA) in the individuals with ASD. Interestingly, there is evidence of both increased and decreased FA relative to the TD group.

Conclusions: The pattern of activity evoked by the ToM cartoons in TD is consistent with previous

evidence that several distinct brain regions are involved in ToM. Furthermore, the different pattern of activity in ASD suggests that there may be differences in the way that this network is organised and functions in ASD. The potential relationship between altered FA and anomalous ToM-related activity in ASD will be discussed.

128.101 101 Language Development among Children with Autism Spectrum Disorders. K. Lopez*[1] and C. Lord[2], (1)*University of Michigan Autism & Communication Disorders Center (UMACC)*, (2)*University of Michigan*

Background: Early communication in children with autism spectrum disorders (ASD) is an important and highly researched topic. However, a particular area that has been underdeveloped for children with ASD is the development of verb production. Given that verb properties influence and direct many other aspects of grammar (Gleitman 1989, Pinker, 1989; Rice and Bode, 1993) it is imperative to research this area of language development. Verb production has been researched among children with normally developing language and children with other developmental disabilities including specific language impairments (). Commonalities have been found between the verb acquisition of children with ASDs and children with other language disorders (Golinkoff, & Hirsh-Pasek, 2008; Rapin & Dunn, 2003; Riches, Tomasello, & Conti-Ramsden, 2005; Shulman & Guberman, 2007). However, the social skills of children with ASDs and children with language disorders are distinctly different, with the former group lacking many typical social behaviors that may explain patterns of verb development. The social skills difference lends itself to be further explored by studies that take both verb acquisition and socialization factors into account.

Objectives: The aim was to explore the language trajectories of children on the autism spectrum (including autism, Asperger's, and PDD-NOS), a group of children and a typical group of children using social affect as a covariate within the models to identify whether social affect contributes to the patterns of language development observed.

Methods: The present study utilizes previously collected data gathered as part of three longitudinal investigations. Ninety children were assessed at multiple time points between 12 and 48 months of age. Language development was measured with the total number of nouns and verbs produced as measured by one of three versions of the MacArthur-Bates Communicative Development Inventory (CDI: Fenson, Dale, Reznick et al., 1993). Social affect was measured with the Autism Diagnostic Observation Schedule (ADOS; Lord, C., Risi et al., 2000).

Results: To assess the language trajectories of verb and noun production among children in each group (autism, PDD-NOS, non-spectrum, typical) HLM 6 multilevel modeling was utilized. Chronological age was used as the primary predictor in the language models. Chronological age was found to significantly predict the number of verbs produced. When added into the basic model, non-verbal IQ (NVIQ), and diagnosis accounted for a portion of the variance explained in the basic model. Social affect did not contribute to the model when included.

Conclusions: The number of nouns and verbs produced by children in the present study was significantly predicted by NVIQ and diagnosis. The language models were similar in their patterns and social affect did not differentiate them. Contrary to previous research (Rapin & Dunn, 2003), the present study indicates that children with autism and with developmental delays are significantly different based on the main effects of diagnosis. Thus, clinical implications include the importance of verb development among children that may be indicative of differential diagnosis in cases that appear similar on the surface.

128.102 102 The Role of Task Support in Spatial and Temporal Source Memory of Adults with ASD. D. M. Bowler*, S. B. Gaigg and J. M. Gardiner, *City University, London*

Background: Bowler, Gardiner & Berthollier (2004) demonstrated intact recognition by adults with ASD of incidentally-encoded sources of studied words such as location on screen, voice of presentation or actions performed on the words. Recall of source, by contrast was diminished in comparison with that of a matched typical comparison group. Source recall difficulties are also seen in multi-list recall paradigms such as the California Verbal Learning test where individuals with ASD make more intrusions from earler-studied lists into the recall of later lists (Bennetto et al, 1996), raising the question of whether support at retrieval would facilitate memory for which list a particular word belonged to at study. We predicted that adults with ASD would benefit from support at test for memory for

the location of studied words on the screen but that support for which block of the word belonged to (first, second or third) would be less effective.

Objectives: To compare the effects of task support at test on memory for spatially and temporally-defined source in adults with ASD.

Methods: 18 adults with ASD and 18 verbal ability matched typical adults took part. Participants studied a list of 27 words consisting of three temporally-distinct blocks of 9 words labelled 'List 1', 'List 2', 'List 3'. Within each block, three words were presented at the top, middle or bottom of the computer screen. Words were presented at a rate of one every 4 seconds with a 6-second pause between each block. The test consisted of a yes/no recognition procedure where studied words were presented randomly interspersed with lures. If participants made a 'yes' response they were either asked to state where on the screen the word had been presented or in which list it appeared (unsupported trials), or to select from source cues (TOP, MIDDLE, BOTTOM or LIST 1, LIST 2, LIST 3) presented on the screen (supported trials). Order of supported and unsupported test and spatial and temporal source were systematically varied.

Results: : Overall recognition memory was similar for both groups, replicating the majority of existing findings on recognition. The source memory data were analysed using a 2 (Group) x 2 (Temporal/Location) x 2 (Support/No Support) ANOVA. There was no group difference in overall source memory, but memory for temporal source was superior to that of spatial source. No other main effect was significant. The only significant interaction was for Group x Source x Support. This showed a marginally superior effect for support for location source in the ASD group but the reverse in the typical group. Presence of support had no effect on temporal source memory in either group.

Conclusions: The findings on the effect of support for memory of source location replicates those of Bowler et al. (2004). The lack of an effect of support for temporal source goes against our prediction and may simply reflect a difficulty in experimentally operationalising temporal cues.

128.103 103 Fast-Mapping in Preschoolers with ASD: The Role of Word Learning Constraints, Imitation, and Joint Attention Skills. A. Williams*, L. G. Klinger, J. Scofield, M. R. Klinger and H. Noble, *University of Alabama*

Background: Fast-mapping is the rapid process by which children learn to link a novel label with a novel referent. Children with typical development (TD) utilize social-cognitive skills (e.g., joint attention, imitation) and word learning constraints (e.g., disambiguation, taxonomic, whole-object) to quickly learn new words. Few studies have investigated word learning in children with autism spectrum disorders (ASD) and the effects that social-cognitive skills may have. It is plausible that children with ASD may be using alternative strategies or skills to learn words due to early symptoms that include language delay and impairments in joint attention and imitation. Objectives: The current study examined the following questions: 1. Do preschoolers with ASD and preschoolers with TD learn words at similar rates? 2. Do preschoolers with ASD utilize word learning constraints to learn new words? 3. What is the relationship between joint attention, imitation, and word learning in preschoolers with ASD? Methods: Participants with ASD were recruited from early intervention preschools. Diagnoses were confirmed using the ADOS-G. Language was assessed by the Mullen Scales of Early Learning. Joint attention skills were assessed by the Early Social Communication Scales and imitation skills were assessed by the Motor Imitation Scale and a verbal imitation measure. Participants with ASD were matched to 2 groups of participants with TD based on chronological age and receptive language. Participants completed 4 word learning conditions: (1) Basic condition examined the ability to link a novel label with a novel object; (2) Disambiguation condition examined the ability to link a novel label with a novel object when it is presented in conjunction with a familiar object; (3) Taxonomic condition examined ability to assume that novel labels extend to objects that are similar in shape; and (4) Whole-Object condition examined ability to assume that novel labels refer to whole objects. All participants completed 4 trials of each word learning condition. Results: Data were collected on 16 children with ASD (mean age = 50 months), 16 children with TD matched on chronological age (mean age = 45 months), and 16 children with TD matched on receptive language raw score from the Mullen. Preliminary analyses show that all 3 groups showed a similar pattern of performance across the word learning conditions. However, children

with ASD had significantly lower joint attention and imitation abilities compared to both TD groups. While joint attention and imitation abilities were related to receptive language in the ASD group, these abilities were not related to performance on word learning conditions. Preliminary analyses are ongoing. Conclusions: Preliminary findings indicate that preschoolers with ASD fast-mapped and utilized word learning constraints in a similar manner to children with TD, despite impairments in joint attention and imitation. Thus, the ability to utilize word learning constraints is intact for children with ASD. The current study supports previous research that shows that joint attention is a predictor of language abilities, and also suggests that joint attention and imitation skills may not be necessary prerequisites for vocabulary development in children with ASD.

128.104 104 Learning in ASDs: Probabilistic Selection and Transitive Inference. M. Solomon*[1], M. J. Frank[2], S. Ly[1] and C. S. Carter[1], (1)*MIND Institute, Imaging Research Center*, (2)*University of Arizona*

Background: Many symptoms that are pathognomic of autism spectrum disorders (ASDs) can be considered to reflect deficits in learning. Although the majority of empirically supported autism interventions are premised on learning theory, there has been little experimental research about this clinically significant topic. One major learning problem for individuals with ASDs is the failure to "generalize" or to transfer past learning to new situations.
Objectives: To examine performance of adults with ASDs on two reinforcement learning tasks that assess processes involved in generalization. In the first, a probabilistic selection (PS) task, three stimulus pairs, AB, CD, and EF were presented in random order. Participants learned to choose one of the two stimuli based on probabilistic feedback following each trial that was accurate 80%, 70%, and 60% of the time. In the second, a transitive inference (TI) task, participants were trained on a partially-overlapping stimulus hierarchy with four pairs: A+B-, B+C-, C+D-, and D+E-. During a subsequent test phase, the novel combinations BD and AE were tested.
Methods: Twenty five participants each were enrolled in the ASD and typically developing (TYP) groups. Sixteen adults with ASDs (Mean age = 22.7) and 17 TYP (Mean age = 23.8) could complete the PS, and 18 (Mean age = 22.4) ASDs and 23 TYP (Mean age = 22.7) could complete the TI. All participants had Full Scale IQs of > 70 on the Wechsler Abbreviated Scales of Intelligence. Participants with ASDs had prior diagnoses and met criteria for ASD on ADOS-G (Lord et al., 2000), and a DSM-IV-R checklist.
Results: Early in probabilistic learning, individuals with ASDs were unimpaired at acquiring the simplest AB stimulus pair, however, they exhibited slower learning for the more difficult CD pair, and deficits using positive feedback. Interestingly, ASDs performed significantly better than TYP on the DE stimulus pair for which accurate feedback was rarely provided. After training on a TI task, individuals with ASDs learned simple stimulus response associations comparably to TYP and exhibited a U-shaped learning curve (better performance on outer pairs compared to inner pairs), which signals efficient use of both associative and elemental learning strategies. At test, there were no significant differences in performance on the novel BD pair, although performance on the AE pair, was significantly worse in the ASD group.
Conclusions: Although, ASDs performed comparably to TYP after training, early in learning they exhibited a pattern of relative impairment and relative strength on the PS task. On TI, they learned the training pairs comparably to TYP and were able to complete the BD pair. Frank et al. (2004, 2005, 2006) have proposed a systems-level computational model of reinforcement learning that focuses on interactions between the basal ganglia and the prefrontal cortex. Taken in the context of this computational model, our findings suggest intact functioning of sub-cortical structures, with deficits in frontal functioning and/or fronto-striatal connectivity. Treatment implications also will be discussed.

128.105 105 Visual Scanning of Dynamic Faces in Relation to Varying Positive and Negative Affect. L. A. Edwards*, W. Jones and A. Klin, *Yale University School of Medicine*

Background: The ability to derive socially relevant information from faces is fundamental to interpersonal communication and reciprocal social interaction. In structured viewing tasks, such as looking at still images of faces showing exemplar emotions, adults with autism exhibit increased fixation to atypical or nonfeature areas of the face (e.g., looking at the cheeks, chin, or hairline rather than at the eyes). And in face recognition tasks as well as when making judgments about facial emotions, individuals with autism show an over-reliance on information from the mouth region as well as increased fixation on the mouth

area. Reduced looking at eyes and increased looking at the mouth have also been observed during natural viewing conditions (i.e., watching dynamic faces in scenes of social interaction). This observation was recently extended from adolescents and adults to 2-year-olds with autism. However, it is not known whether these children's visual fixation patterns are impacted by varying facial affect.

Objectives: This study examines visual fixation patterns in toddlers with autism during viewing of dynamic faces displaying a range of naturally-occurring positive and negative affect.

Methods: Two-year-olds with autism spectrum disorders and control children matched on age-, verbal-, and nonverbal function, watched video scenes of female actors playing the role of caregiver and displaying a range of facial expressions. Dynamic facial expressions in the caregiver videos were quantitatively ranked by naïve external observers for degree of positive vs. negative affect. Then, using the ratings of affect as an analytic regressor, we examined the eye-tracking data in relation to varying degree of naturally-occurring facial affect.

Results: Preliminary results suggest that the emotional valence of dynamic faces alters visual fixation patterns in two-year-old, typically-developing children. In two-year-olds with autism, however, facial expressions have little impact on visual scanning. Across varying social affect, two-year-olds with autism look less at the eyes of others, while looking more at others' mouths.

Conclusions: Differential attention to faces, particularly in conditions of changing affect, is critical for extracting information about the intentionality of others. Failure to do so suggests an altered path for learning about the surrounding world, with potentially profound impact on subsequent social development. Over the course of development, failing to reallocate visual resources in a manner that is contingent with changing facial affect is likely to exacerbate increasingly atypical neural specialization, altering the formation of the social mind and brain.

128.106 106 Intentional Communication in ASD: Quantitative and Qualitative Distinctions from Typical Development?. J. P. W. Maljaars*[1], I. L. J. Noens[2], R. M. Jansen[1], E. M. Scholte[1] and I. A. van Berckelaer-Onnes[1], (1)*Leiden University*, (2)*Katholieke Universiteit Leuven*

Background: In literature often is stated that children with an ASD initiate communication less frequently compared to typically developing children, both to regulate behavior of others and to share objects and experiences with others (joint attention). Furthermore, when children with an ASD do communicate, they rather communicate for behavior regulation than for social purposes, such as joint attention (e.g., Landa, 2007; Wetherby et al., 2007; Dawson et al., 2004). However, it is still unclear whether these differences are just quantitative or also qualitative by nature.

Objectives: To explore quantitative and qualitative differences in functions of intentional communication and the forms used to communicate for these functions between children with the autistic disorder and typically developing children.

Methods: Data were collected from 20 children with the autistic disorder (confirmed by the ADOS and the DISCO-11) and 20 typically developing children. Both groups were matched on non-verbal intelligence level (developmental age range: 2;0–5;0 years), measured with the Snijders-Oomen Non-Verbal Intelligence Test – Revised (SON-R 2½-7). Videotapes of the Communication and Symbolic Behavior Scales (CSBS-DP Behavior Samples; Wetherby & Prizant, 2002) were analyzed using a standardized observation scheme distinguishing three main functions: behavior regulation, social interaction, and joint attention. Also different forms were inventoried: vocalizations, gestures and other acts.

Results: Preliminary results (n=13 AD, n=13 TD) indicate that children with the AD show significantly less intentional communicative actions than typically developing children, in particular with regard to declarative goals (social interaction and joint attention). There is no significant difference in the relative frequencies of communicative behaviors for these functions. Furthermore, typically developing children communicate more frequently for declarative goals compared to behavior regulation, whereas children with the AD communicate for each goal just as often.

Conclusions: In absolute frequencies children with the AD seem to communicate less often for declarative purposes compared to typically

developing children. However, they do not show a more restricted repertoire of communicative functions, as the relative frequency of functions for which the children of both groups communicate is almost identical. These preliminary findings suggest that the differences between both groups are mainly quantitative and not qualitative by nature.

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128.107 107 Relation Between Language and False Belief Performance in High Functioning English Speaking Children with Autism. H. Seung*[1], H. Lee[2] and J. Farrar[3], (1)*California State University*, (2)*Yeung Nam University*, (3)*University of Florida*

Background:

False belief tasks are one method of assessing Theory of Mind. The role of language in false belief has been studied; in particular English complementary structure and vocabulary understanding have been evaluated (deVilliers, 2005; Tager-Flusberg & Joseph, 2005).

Objectives: This study attempted to examine which aspect of language might predict false belief task performance in children with high functioning autism. The predictors examined were chronological age, comprehension of: mental verb (Think) and communication verb (Say), and relative clause, and receptive vocabulary. This was a part of larger study funded by the Korea Research Foundation. The larger study is a cross-linguistic comparison between English- and Korean-speaking children.
Methods: Twenty children with high functioning autism (age between 5 and 11 years) and 20 children with language delay without autism (age between 3 and 6 years) will participate in this study. Data collection has completed so far with sixteen English speaking children with high functioning autism (Mean=7.6 years). Each participant received an IQ test (K-ABC-II) and a receptive vocabulary test (PPVT-4). All participants had IQ scores higher than 70. The ToM task consisted of unexpected location (FBL), unexpected content (FBC), language task (Say and Think) tasks. These were presented on a laptop computer while the examiner presented brief stories that corresponded to the pictures and asked questions.

Results: Preliminary data from the first 16 participants with autism was analyzed using multiple regression analyses. After controlling for age (R^2=.44, F (1, 14)=10.87, p=.005), the regression equation with the Think was significant, R^2 change=.22, F (1, 13)=8.51, p=.012. However, the regression equation was not significant with either Say, R2 change=.00, F (1, 12)=.02, p=.897 or Relative Clause (RC) comprehension, R^2 change=.03, F (1, 11)=1.12, p=.312. Also the regression equation with the PPVT was significant, R^2 change=.13, F (1, 10)=7.44, p=.021.
Table 1. Regression analysis using language as predictors.

step	variable	B	SE	b
1	age	1.06	.32	.66**
2	Age	.72	.28	.45*
	Think	1.23	.42	.52*
3	Age	.71	.30	.45*
	Think	1.20	.52	.50*
	Say	.06	.51	.03
4	Age	.71	.30	.44*
	Think	1.18	.51	.49*
	Say	.01	.51	.01
	RC	2.33	2.2	.18

5	Age	.78	.24	.49**
	Think	1.20	.41	.50*
	Say	-.51	.45	-.22
	RC	.10	1.93	.008
	PPVT	.08	.03	.46*

Step 1, R^2=.44, F (1, 14)=10.87, p=.005

Step 2, R^2=.66, DR^2=.22, F (1, 13)=8.51, p=.012

Step 3, R^2=.66, DR^2=.00, F (1, 12)=.02, p=.897

Step 4, R^2=.69, DR^2=.03, F (1, 11)=1.12, p=.312

Step 5, R2=.82, DR^2=.13, F (1, 10)=7.44, p=.021

Conclusions: The preliminary results indicate that age, mental verb (Think) comprehension, and receptive vocabulary predicted the false belief performance. Results of this study are consistent with de Villiers and Pyers (2002) who proposed that the complement structure comprehension is critical in understanding false belief tasks.

128.108 108 The Shape Bias: Investigations of Word Learning with Children with Autism. G. Jaffery, S. Tek*, J. Piotroski, J. Rodny, D. Fein and L. Naigles, *University of Connecticut*

Background: The shape bias is a word learning mechanism that young children use to map the referent of a novel noun onto the shape of a novel object, rather than onto its color, texture, or size. Previous research has demonstrated that, unlike typical children, young children with autism up to four years of age do not use the shape bias as a word learning mechanism even though they have acquired a sizeable lexicon (Tek et al., 2008). Objectives: In the current study, we investigate whether these children developed a shape bias at a later age; moreover, we performed more detailed analyses of their shape bias performance. Methods: We tested 18 typically developing toddlers (mean age = 20.62 months at the onset of the study) every four months over four time points, and 17 children with autism (mean age = 33.13 months at onset) over six time points. The children had been matched on expressive vocabulary at Visit 1. We used the preferential looking paradigm, in which we presented novel target objects with two alternative test objects: one matching the target in shape and one in color. During the first set of trials, the NoName (baseline) audio asked "which one looks the same?" During the second set of trials, the target was given a novel label and the Name (test) audio asked "which one is (novel name)?" The dependent variables included (a) percent looking to the same-shape object, (b) the latency between the presentation of the test audio and subjects' looking to the shape-match, (c) the number of switches of attention between the shape-match, the color-match, and looking away, and (d) the direction of first look to either the shape match or the color match. We also created time-course graphs to investigate children's patterns of looking to the shape match, color match, and away during the span of every trial. Results: The typical group looked significantly longer at the shape match during the Name trials for Visit 2 through Visit 4 ($p < .05$), whereas the ASD group showed no such preference, even at the last visits. However, the ASD children did seem engaged in the task: Children in both groups had longer latencies of looking to the shape match during Name trials than during NoName trials ($p < .05$), showing that determining which of the test objects has the same label as the target requires longer and more conscious processing than simply determining perceptual similarity. The timecourse graphs revealed that, during Visits 3 and 5, the ASD group did tend to prefer the shape match during the last 3 seconds (50%) of each Name trial; however, this tendency disappeared during Visits 4 and 6. None of the other measures yielded significant results. Conclusions: These results support our previous finding that children with autism have difficulty using the shape bias as a word learning mechanism. The difficulty is not attributable, though, to lack of engagement in the task.

128.109 109 Cues to Word Learning in Autistic Spectrum Disorders. C. Norbury*[1], H. Griffiths[2] and K. Nation[2], (1)*Royal Holloway, University of London*, (2)*University of Oxford*

Background: Cognitive theories of autistic spectrum disorder (ASD) predict difficulties in acquiring new words either because of deficits in attending and/or processing social cues, or deficits in using linguistic context to infer word meaning. However, studies of word learning have focused exclusively on 'fast-mapping' abilities; we know little about learning the phonological and semantic features of new words over time. In addition, we cannot be sure why children with ASD fail to interpret social or linguistic cues because previous

studies have only been able to focus on the end product of learning rather than the process itself.

Objectives:

1) to investigate learning of novel words over multiple trials and over time in children with ASD relative to peers
2) to determine whether words are more easily learned in social versus linguistic contexts
3) to determine how children with ASD utilize social or linguistic cues to word learning using eye-tracking techniques

Methods: Our participants included 13 children with ASD, 13 children with language delay and 13 typically developing children (aged seven years). Children saw three novel objects on a computer screen and clicked the photo that matched a spoken sentence. In the social cue condition, a female gazed at the target item. In the linguistic cue condition, information in the sentence biased a particular interpretation. We recorded children's eye-movements as they completed the task. Immediately after the experiment and approximately four weeks later, we assessed word learning via word recognition, definition and naming tasks.

Results: In the recognition task, all participants identified more words learned with social cues than linguistic cues. Similarly, all groups provided more semantic information in definitions for items presented in the social condition, even though semantic information was explicitly stated in the linguistic condition. In the naming task, there was an interaction between group and cue type such that participants with ASD were better at recalling phonological information for words presented with social versus linguistic cues, whereas type of cue did not affect performance in the comparison groups. We are currently analysing eye-tracking data, focusing on the hypothesis that children with ASD are able to devote more processing resources to phonological information in the social cues condition because they do not spend as much time studying the social cue (i.e. the face) as much as peers.
Conclusions: Our results indicate that social cues such as eye gaze and head turn are particularly salient cues for word learning, even for ASD participants. More semantic information was recalled in the social cue condition, suggesting the possibility that social cues are mapped quickly, leaving more time to encode visual features of novel objects. The most notable finding of this study is that children with ASD were better than peers at phonological aspects of word learning, especially when words were presented with social cues. Our eye-tracking analyses will enable us to determine whether success on this task is the result of devoting more attention to sound than meaning. We consider these findings as an alternative mechanism for acquiring vocabulary in ASD.

128.110 110 Vocal Prosody in Autism: Understanding the Effects of Enhancing Vocal Prosody on Children's Comprehension and Retention of Story Narratives. L. M. Black*[1], J. P. H. van Santen[1], R. Coulston[1], J. de Villiers[1] and R. Paul[2], (1)*Oregon Health & Science University*, (2)*Yale University School of Medicine*

Background: Therapists working with children with Autism Spectrum Disorders (ASD) frequently adjust the way they speak to what helps the individual child, often manipulating their vocal prosody and expressivity to better engage the child and help him focus as well as to process information better. Typically, therapists are unaware that they are doing so. Research to date on intervention outcomes with ASD children has never focused on the benefits of enhancing expressivity, whether in voice, face, or gestures. In fact, very few intervention approaches use highlighting of affect or expressivity as a specific strategy for ASD. (Greenspan & Wieder's DIR/Floortime and Gutstein's RDI do, but for these approaches, there is a paucity of outcome research.) It may well be, however, that enhancing prosody may be a key strategy to help children with ASD. Objectives: The purpose of the study was to measure the effects of prosodic style, specifically enhancement of vocal prosody, on narrative recall performance in children with ASD vs. Typical Development (TD). Results on a small number of participants were reported at IMFAR, 2008. The present study is a continuation of the previous one, with more subjects having now been seen. Methods: Seventy-nine participants (ages 4-8) underwent diagnostic and neurocognitive assessment. Thirty-seven children were classified into the ASD group; forty-two into the TD group. Two stories were developed about interpersonally dynamic and affectively-charged events, rich in factual and social cognitive information. They were produced in three prosodic modes. (E) Enhanced, (S) Standard, (D) Disconnected. In E, prosody highlighted story content and meaning at multiple levels (using

affective, pragmatic, and grammatical prosody). S used typical prosody. In D, words were recorded randomly, concatenated into sentences, and acoustically modified to have continuous pitch and energy contours. Additional signal modification methods were used to match all modes on average pitch, energy, speaking rate, and pause duration. Separate questions were developed for factual and social-cognitive aspects of the story. Results: ANOVA analysis, with Prosodic Mode (E vs. S vs. D), Group (ASD vs. TD), and Story as independent variables, resulted in a significant interaction between Group and Prosodic Mode, with ASD children significantly better able to answer narrative questions as prosody intensity increased from D to S to E; no such beneficial effect of prosodic mode was seen for TD. Trends were found for this interaction to be more pronounced for the social cognitive questions. TD performed better than ASD in all prosodic modes; but in E compared to D, the TD-ASD difference was significantly reduced. Conclusions: These results extend and confirm the findings from a smaller group of ASD and TD children reported in 2008. They suggest that enhanced prosody specifically targeted to highlight the multiple levels of information in complex verbal communication helps comprehension and retention of information in children with ASD, in particular, social cognitive information. This has important implications for intervention as well as for assessment.

128.111 111 Use of Written Diaries in Tracking the Language Development in Infants at Risk for ASD. Y. Tsai*[1], L. Kasparian[1], L. M. Casner[2], A. S. Carter[3] and H. Tager-Flusberg[1], (1)*Boston University School of Medicine*, (2)*Boston University*, (3)*University of Massachusetts Boston*

Background:
Parental reporting has been viewed as an important source of information in studying the development of infants who are later diagnosed with ASD. However, retrospective parental reporting can be affected by distortion of recall. Therefore, as an alternative, written diaries may be used to collect data frequently during the early stages of development in order to identify delays in language and communication as they develop.

Objectives:
To examine the effectiveness of written diaries as a novel approach for studying the development of infants at risk for ASD.

Methods:
In an ongoing study, there are three groups of participants ¾infants at risk for ASD, infants at risk for specific language impairment (SLI), and typically-developing controls. Parents were asked to complete written diaries on a weekly basis, either though an online database or on paper, beginning when their infant turned 6 months old, and continuing until their infant reached 18 months of age. Parents were also asked to complete monthly home video diaries during this age range as well as come into the laboratory to be seen with their infants at 6, 9, 12, 18, 24 and 36 months.

Results:
On average, ASD-risk families (n=31) submitted 11.7 diaries each throughout the 12-month period, SLI-risk (n=6) families submitted 23 diaries each, and control families (n=24) submitted 11.7 dairies each. Preliminary analysis suggests that all three groups developed consonants within the age range of 7 to 9 months. ASD-risk infants who were later diagnosed with ASD developed words about 3 months later than ASD-risk infants who did not receive diagnoses. Parents of ASD-risk infants also expressed more concerns than parents of SLI-risk infants and parents of control infants. Ongoing work will focus on the differences found in the diaries between ASD-risk infants who later meet criteria for ASD and ASD-risk infants who do not meet criteria for ASD. The correlation between behaviors reported by parents and behaviors seen in standardized assessments will also be evaluated.

Conclusions:
Thus far, our results suggest that families are capable of completing at least one written diary per month, enabling us to collect data more frequently and in a cost-effective way. Written dairies may also help us to identify delays in language development in ASD-risk and SLI-risk infants.

128.112 112 Neuropsychological Characteristics of School-Age Children with High Functioning Autism, PDD-NOS and Asperger Syndrome: Performance On the NEPSY-I. P. Cavolina[1], G. Doneddu[1], C. Urgesi[2], I. Obbili*[1], R. Fadda[3] and V. Manunza[1], (1)*A.O.B. (Azienda Ospedaliera Brotzu)*, (2)*Faculty of Educational Sciences*, (3)*University of Cagliari*

Background: A primary aim of recent research has been to define the specific neuropsychological profile in Autism Spectrum Disorder (ASD), in

order to delineate appropriate types of interventions aimed to enhancing cognitive capacities in individual with autism (Hooper et al., 2006). However, little is still known about the neuropsychological characteristics of children with HF autism, PDD-NOS and Asperger syndrome, who usually have adequate cognitive abilities compared with controls.
Objectives: On the basis of these consideration our study aimed to profile neuropsychological characteristics in HF autism, PDD-NOS and Asperger syndrome across a range of neuropsychological tasks, compared with a group of controls matched for mental age.
Methods: 30 participants with ASD (8 HF Autism; 11 PDD-NOS; 11 Asperger syndrome; 26 males; 4 females; aver.chron.age= 8,7 yrs; DS 2; aver. IQ = 90; DS =13,3) and 56 ND children (35 males; 21 females; aver.chron.age= 7,8 yrs;DS= 1,8) were asked to performe in a range of neuropsychological tasks (Nepsy-I) measuring memory of faces, memory for names, visual attention, fingertip tapping, imitating hand position and visuomotor precision.
Results: The results showed that children in the three atypical groups were lower than controls in the Sensory Motor Functions domain. PDD-NOS were better than controls in Visual Attention (PDD aver. scores = 8.55; DS=2.4 - ND aver. scores = 6.4; DS= 2.1 – F=0,559; df=65; p=0.004) and in Memory of face (PDD aver. scores = 9.6; DS=4.1 - ND aver. scores = 7; DS= 2.5 – F=1.3162; df=65; p=0.009). The Asperger group was higher than controls only in Memory of face (Asperger aver. scores = 9.9; DS=4.5 - ND aver. scores = 7; DS= 2.5 – F=10.025; df=65; p=0.005).
Conclusions: In line with previous research, the neuropsychological profile of the children with ASD was, in general, characterized by a weakness of sensory motor functioning. The performances in some tasks of the Nepsy-I contributed to define a more specific profile for each single diagnostic group, underling the strengthens of the Asperger and PDD-NOS groups. These different profile might be used to develop individualized programs who might improve the effectiveness of the intervention.

128.113 113 Expressive and Receptive Language Impairment in Young Children with Autism. M. D. Bomba* and E. W. Pang, *Hospital for Sick Children*

Background: Autism is a developmental disorder involving primary impairments in both language and communication. Language difficulties vary widely in the autism population and improving our understanding of these problems is key to furthering our understanding of autism. Language deficits are often one of the first presenting symptoms **[1, 2]** and certainly are one of the most important features for predicting the prognosis and developmental course for children with this disorder **[3, 4]**.

Objectives: The goal of this study was to investigate the presence and extent of language deficits in children with autism compared to healthy age-matched controls. In broad terms, language can be divided into two processes: receptive language which involves the processing of incoming language information; and expressive language, which involves producing language either by speaking or writing.

Methods: We investigated expressive and receptive language functioning in a group of 17 children (14M/3F; 3-8 yrs of age) diagnosed with autism using the ADOS and ADI-R, and meeting DSM-IV criteria, compared to a group of healthy age-matched controls (n=30; 11M/19F). The children with autism had some verbal ability, normal hearing and no co-morbid neurological or psychiatric diagnoses. To determine whether there were differences in expressive and receptive language abilities between children with autism and control children, standardized language tests were administered to both groups. Depending on their age and ability, children were tested using the OWLS (Oral and Written Language Scale), PLS-3 (Preschool Language Scale) or CELF-3 (Clinical Evaluation of Language Fundamentals).

Results: Among the children with autism there was heterogeneity in their language skills, although across the entire group of children, articulation skills were spared. Compared to healthy children, children with autism scored significantly lower in both expressive (p=0.0001) and receptive (p=0.0001) language domains. Compared to one another, children with autism showed no significant receptive-expressive differences. Interestingly, we did not find significant differences between the younger (defined as 3-5 yrs) and older children (6-8 yrs) with autism in this study. This is consistent with other studies **[5, 6]** although our inclusion of a large control group further substantiates the literature.

Conclusions: Our findings confirm that children with autism also have language deficits that need to be addressed and monitored to enhance effective communication in everyday life. This finding replicates and extends, as well as supports, the hypothesis that autism and speech and language impairments may be linked etiologically **[5, 7]**.

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128.114 114 Are Language Abilities Related to Early Social Aptitude in Young Children with and without Autism Spectrum Disorders?. L. O'Connell*, K. A. Dunfield, E. A. Kelley and V. Kuhlmeier, *Queen's University*

Background: The interrelationship between early language development and an infant's social world in typically developing (TD) children is well established (e.g., Brooks & Meltzoff, 2005; Carpenter, Nagell, & Tomasello, 1998; Aktar et al., 1991). For children with Autism Spectrum Disorders (ASD), who are often noted as having language difficulties, the extent of the impact of such a relationship on social development beyond the first few years of life is of particular importance.

Objectives: Using measures of expressive and receptive language, the current study examined the relationship between children with and without ASD's language abilities and their engagement in a series of social-cognitive and prosocial tasks. Importantly, the social tasks required minimal verbal understanding. A measure of children's nonverbal mental age was also obtained to account for differences in cognitive ability.

Methods: Children with ASD (N=11) and a group of TD children matched on nonverbal mental age (N=10) (Nonverbal Mental Age range 19-69 months) were assessed for their language abilities. All children engaged in the *Mullen Scales of Early Learning* (*MSEL*; Mullen, 1995) to obtain a measure of both receptive and expressive language. Additionally, the visual reception subscale of this test provided an index of children's nonverbal mental age. Children's communication skills beyond the laboratory were evaluated via the administration of the *Vineland Adaptive Behaviour Survey* (*VABS*; Sparrow, Cicchetti, & Balla, 2005) to primary caregivers. Children also participated in a series of play-based tasks designed to examine several social-cognitive skills (joint attention, imitation of bodily movements and actions on objects, intentional understanding). Participants were also presented with several social scenarios in which they were evaluated for their tendency to provide different types of aid to the examiner (i.e., retrieving and out-of-reach object, overcoming a physical obstacle, comforting, and sharing). Children with ASD attended the lab on a second occasion to confirm an Autism Spectrum diagnosis using the *ADOS.*

Results: Data collection will continue until each group includes 15 children. Using existing data, the relationship between children's language abilities and their engagement in early social-cognitive behaviour was examined via a series of partial correlations. After controlling for nonverbal mental age, there was no relationship between children's language abilities and overall social-cognitive performance in either group. The analysis of language in relation to prosocial behaviour yielded different results. There was no association between language abilities and overall prosocial performance in the ASD group. Conversely, TD children's expressive language skills (*MSEL*) were positively associated with their overall demonstration of prosocial behaviour (r=.82, p<.01).

Conclusions: The association between language and social development during the preschool years

appears to exist differentially in TD children and those with renowned language challenges, namely children with ASD. Rather than the mutually beneficial existence of language and social interaction, children with ASD appear to rely on mechanisms beyond language for social skill development. Conversely, given their relatively strong social performance paired with poorer language skills displayed here, the results suggest that children with ASD may not reap the language benefits of social engagement as do TD children.

128.116 116 Cognitive Functioning and Adaptive Behavior in Children with Autism. M. Al Darwish*, L. LaRose and R. Nicolson, *The University of Western Ontario*

Background: Studies have consistently demonstrated deficits in adaptive functioning in children with autism spectrum disorders, particularly in the areas of communication and socialization. These deficits remain even when children with autism spectrum disorders are compared on measures of adaptive functioning after controlling for potential confounding effects related to intelligence. However, the nature of the relationship between intelligence as measured by standard tests and adaptive functioning in children with autism spectrum disorders remains uncertain.

Objectives: The purpose of this study was to compare the correlations between full-scale and sub-scale measures of IQ and socialization scores on the Vineland Adaptive Behavior Scale in children and adolescents with autism spectrum disorders.

Methods: Thirty-three children and adolescents with an autism spectrum disorder (2 females) and 37 children and adolescents with a non-autism spectrum psychiatric diagnosis (8 females) were assessed with the Wechsler Intelligence Scale for Children, Fourth Edition (WISC-IV) and the Vineland Adaptive Behavior Scales, Second Edition (Vineland-II). Correlations between the WISC-IV full-scale and subscale (verbal comprehension, perceptual reasoning, working memory, processing speed) standard scores and Vineland II Socialization scores (including the subscale scores for interpersonal relations, play and leisure, and coping skills) were calculated and compared between groups.

Results: The two groups did not differ significantly on any WISC-IV scores. However, patients with autism had a significantly lower correlation between their WISC-IV verbal comprehension and Vineland-II interpersonal skills scores (r=-0.05) than non-spectrum controls (r=0.05; p<0.05). At the same time, patients with autism had a significantly higher correlation between their WISC-IV perceptual reasoning and their Vineland-II socialization scores (r=0.4) than non-spectrum controls (r=0.2; p<0.05).

Conclusions: Unlike non-autism spectrum psychiatric controls, interpersonal skills in children and adolescents with autism spectrum disorders are best predicted by their perceptual (non-verbal) IQ scores. These findings suggest that examining interpersonal skills scores from the Vineland in the context of verbal and non-verbal intelligence scores may be of benefit in clarifying the diagnosis of autism spectrum disorders and may further our understanding of the social deficits in these disorders.

128.117 117 Selective Attention and Emotion Self-Regulation Are Critical in Classroom Pro-Social Behavior. M. Levine*[1], R. J. Calvanio[2] and G. Mesibov[3], (1)*SymTrend, Inc.*, (2)*Massachusetts General Hospital*, (3)*University of North Carolina at Chapel Hill*

Background:

In a previous IMFAR poster we reported that a positive emotional state is an important determinant of pro-social classroom behavior in children with Asperger's Syndrome (AS) or High Functioning Autism (HFA). This finding, however, does not indicate: 1) how the emotional impact upon classroom behavior is mediated in cognitive terms; 2) what other factors supplement emotion as behavioral determinants; and 3) what influence specific autistic traits have on classroom behavior. Thus, our earlier finding (NIMH 1-R41-MH075162-01) provides only limited direction for formulating an intervention to optimize positive classroom behavior.

Objectives:

The objectives of the present study (NIMH 2-R42-MH075162-02) were twofold: 1) to replicate the previous findings regarding the impact of emotion on classroom behavior in a larger more diverse AS population and 2) to answer the questions listed above that emerged after our previous study.

Methods:

Participants were teens (13-19), diagnosed as AS/HFA, who had full scale IQs greater than 75 and attended a middle or high school inclusion program. The AS/HFA diagnosis was verified by the parent Social Responsiveness Survey (SRS). Teachers completed the BRIEF, which provides indices of attention and executive functioning. Trained observers reported emotional expression and social behavior in classroom settings. The in vivo measures of emotion were: happy/sad, peaceful/angry, interested/bored, calm/nervous, confident/overwhelmed, awake/sleepy, and "Engine Speed". The in vivo social behavior measures were: cooperation with teachers, interaction with peers, self-expression, self-control, attention to instruction, social pragmatics during class discussion and inflexibility. During the five-week baseline period, the observers recorded these indices three times per week in three classes using Palm handheld computers and software from symtrend.com.

Results:

1) Classroom emotional status was strongly correlated with classroom social behavior, replicating previous results: $r=0.81$, $p<0.0001$). 2) The BRIEF's behavior regulation index – which reflects inhibitory and set shifting ability – was correlated with two in vivo measures of emotional expression: happy/sad ($r=-0.40$, $p=0.02$) and peaceful/angry ($r=-0.40$, $p=0.02$). It was also correlated with in vivo measures of classroom behavior: cooperation with teachers ($r=-0.45$, $p=0.01$) and self-control ($r= -0.43$, $p=0.02$). This pattern suggests how cognition mediates the emotional impact upon classroom social behavior: depressive emotion (sadness and anger) is an emotional burden from which students cannot effectively disengage (i.e., inhibit or shift away from). This disengagement failure diminishes cooperation and appropriate class engagement. 3) The BRIEF index of supervisory attention was correlated with certain aspects of classroom social behavior, but not with classroom emotional expression (the metacognition index was correlated with cooperation: $r=-0.37$, $p=0.04$; but not the average of classroom emotions: $r=-0.24$, $p=0.20$). This correlation pattern suggests that supervisory attention supplements the impact of emotional expression as a determinant of classroom social behavior. 4) The only AS trait that correlated with classroom social behavior was inflexibility – a symptom of diminished executive control (e.g., inflexibility – cooperation: $r=0.58$, $p=0.003$), continuing the theme of the previous findings.

Conclusions:

Our results suggest that interventions for improving classroom social behavior should focus on addressing regulation of emotions and supervisory attention/executive control as the route to improving classroom social behavior.

128.118 118 Language, Auditory Attention/Working Memory, and Adaptive Outcome in Children with Autism Spectrum Disorders. K. K. Powell*[1], D. O. Black[2], G. L. Wallace[2], J. L. Sokoloff[1] and L. Kenworthy[1], (1)*Children's National Medical Center*, (2)*National Institute of Mental Health, National Institutes of Health*

Background:

Loucas and colleagues (2008) recently found weaker scores on receptive language measures for individuals with autism as compared to those with specific language impairments (SLI). These poorer scores were driven by difficulties with the Concepts and Directions subtest of the CELF. Loucas and colleagues argue that the linguistic demands of the task compounded by the heavy demands placed on auditory attention and short-term auditory memory may be factors contributing to poorer performance. Since refining how these variables impact adaptive functioning may have implications for treatment priorities, this investigation attempts to disambiguate the role that language ability, and auditory attention/working memory play in the functional use of language and social interaction in high functioning children with autism.

Objectives:

To examine the influence of core language and auditory attention/working memory on adaptive functioning, in a sample of high functioning ASD.

Methods:

Subjects were a clinically referred sample of 41 children (mean age: 9.46 ± 2.98 years; 85.4% male; verbal, nonverbal or full scale IQ≥70) diagnosed with an ASD based on the Autism Diagnostic Interview and/or Autism Diagnostic Observation Schedule, and clinical impression. All data were collected during a comprehensive clinical diagnostic and neuropsychological evaluation. Parents of subjects were interviewed using the Vineland Adaptive Behavior Scale (VABS). The VABS was used to measure functional communication and socialization.

Auditory attention/working memory was assessed with the Wechsler Digit Span subtest, and core language abilities were estimated from a sentence repetition task. Data were analyzed using partial correlations, controlling for age. A follow-up regression including sentence repetition, digit span and age was calculated to examine the unique contribution of each predictor.
Results:
Both sentence repetition (pr= .48, p= .002) and Digit Span (pr= .354, p= .025) scores were correlated with VABS Communication scores but were unrelated to VABS socialization. A follow-up regression including sentence repetition, digit span, and age to predict adaptive communication indicated sentence repetition (p= .026) and age (p= .013), but not digit span (p= .663), were related to adaptive communication.
Conclusions:
We find that estimates of both language ability and auditory attention/working memory are significantly related to communication outcome. Furthermore, when trying to understand the unique contribution of working memory/ auditory attention and core language abilities it appears that core language is a primary predictor of adaptive outcome. Potential implications for treatment include emphasizing the importance of remediating core language abilities, even in high functioning children, with ancillary interventions supporting nonlinguistic auditory processing in order to enhance functional comprehension of spoken language.

128.119 119 The Impact of Bilingual Exposure on the Expressive Language of Children with Autism Spectrum Disorders. C. Hambly*[1] and E. Fombonne[2], (1)*Montreal Children's Hospital*, (2)*McGill University*

Background: Many parents and clinicians assume that early bilingual exposure negatively impacts language development, especially for children with ASDs. This belief persists despite the fact that studies of bilingualism in normal and language-impaired children have not found differences in the ages at which early language milestones are reached or in total spoken vocabulary size between children from monolingual and bilingual environments.

Objectives: To compare major early language milestones and current spoken vocabulary size in children with ASDs from monolingual and bilingual environments.

Methods: Families with a child aged 18 months to 6 years of age diagnosed with an ASD were recruited from Quebec and Ontario (target N=110). Phone interviews were administered to families and included a detailed caregiver language history, questions from the Autism Diagnostic Interview-Revised, and the Vineland Adaptive Behavior Scales-II; these measures generated an estimate of their child's language exposure and also described developmental history and current general function. Families also completed questionnaires including the MacArthur Communicative Development Inventories (Words and Sentences; available in 10 languages). Expressive vocabulary size for children from bilingual environments was calculated both in their dominant language and across languages by summing concepts labeled by a word in one or both languages (total conceptual vocabulary).

Results: Children were first classified into monolingual (MON) or bilingual (BIL) groups based on exposure to one or two languages from birth to age 2, with a significant difference in estimated language exposure between the groups (MON mean = 100%, BIL = 64%; SD 20%, p=<.01). Groups were comparable in age (MON=57 months, BIL=58) and demographic variables (parental education, family income). Data analysis (MON N=27, BIL N=20) revealed no significant differences between the groups' mean age in months at first words and first phrases. Family concern regarding a child's development occurred at the same mean age, but the age at which the possibility of an ASD was first discussed with a professional differed significantly, with families from bilingual environments reporting the first discussion 6 months later than monolingual families (31.5 vs. 25.1 months; p <.01, 95% CI 1.4-11.3). A second analysis compared current expressive vocabulary size. Children were re-grouped based on lifetime exposure to a second language, with >10% average lifetime exposure required to be considered bilingual; no significant differences in age (57 vs. 58 months) or demographic variables were noted. The groups did not differ significantly on either their vocabulary in their dominant language (MON=369 vs. BIL=394 words spoken) or in their total conceptual vocabularies (369 vs. 429 words).

Conclusions: These data do not support a significant relationship between bilingual

environments and additional language delay in children with ASDs. The data, however, do suggest that parents and/or professionals may assume that bilingual environments contribute to a language delay, and thus do not consider an ASD diagnosis even when early concerns are present.

128.120 120 Lie-Telling, Theory of Mind, and Verbal Ability in Children with ASD. A. S. Li*[1], E. A. Kelley[1], A. D. Evans[2] and K. Lee[2], (1)*Queen's University*, (2)*University of Toronto*

Background:

The ability to tell lies requires understanding that others may have mental states that differ from one's own and that mental states drive behaviour. Though many studies have demonstrated that individuals with ASD have a deficit in ToM, researchers have just begun to examine lie-telling abilities in individuals with ASD. Furthermore, many studies have found a relation between ToM and language (e.g., Fisher, Happé, & Dunn, 2005); however, no published studies to date have considered the possible contribution of verbal ability when examining the relation between ToM and lie-telling in children with ASD.

Objectives:

The purpose of this study is to examine the interrelations among lie-telling behaviours, ToM understanding, and verbal ability in children with ASD.

Methods:

Our preliminary sample (testing is ongoing) consists of 24 TD children (CA: M = 7.17, SD = .72; VMA: M = 7.59, SD = 1.30) and 10 children with ASD (CA: M = 8.07, SD = 1.12; VMA: M = 7.48, SD = 1.32). Antisocial lie-telling is assessed using a temptation resistance paradigm (Talwar & Lee, 2002) in which children are asked not to peek at a toy while the experimenter leaves the room and then asked upon the experimenter's return if they peeked at the toy. They are also asked questions to examine their ability to maintain consistency between their lie and subsequent statements (i.e., semantic leakage control). Prosocial lie-telling is assessed using a modified version of Talwar, Murphy, and Lee's (2007) undesirable gift paradigm in which children receive a disappointing prize from the experimenter and are asked if they like their prize.

ToM understanding and verbal ability are assessed using a battery of standard first- and second-order false belief (FB) tasks and the core battery of the *Clinical Evaluation of Language Fundamentals–Fourth Edition*, respectively.

Results:

Based on the 14 TD children and 7 children with ASD that peeked at the toy, the groups do not differ on antisocial lie-telling and semantic leakage control. Surprisingly, children with ASD may be more likely than TD children to tell prosocial lies ($\chi^2(1) = 3.52$, $p = .06$).

Verbal ability in children with ASD is not correlated with first-order FB understanding, but it is correlated with second-order FB understanding ($r(10) = .70$, $p = .02$). It was hypothesized that lie-telling would be correlated with ToM understanding and verbal ability in children with ASD; however, due to the lack of variability in the current sample—100% of peekers told antisocial lies and 100% of children told prosocial lies—this hypothesis remains to be tested. Semantic leakage control is correlated with ToM understanding in TD children ($r(12) = .60$, $p = .04$); however, it is not correlated with ToM understanding or verbal ability in children with ASD.

Conclusions:

Our preliminary findings demonstrate that high-functioning children with ASD have little difficulty telling antisocial and prosocial lies, which suggests they may have at least a rudimentary ToM. However, children with ASD may be using different processes than TD children when deciding when and how to deceive others.

128.121 121 Efficacy of a Prompted-Pointing Therapy in Improving Learning Behavior in Non-Speaking Children with Autism. G. M. Chen*[1], B. A. Ganzel[1], M. S. Goodwin[2] and M. K. Belmonte[1], (1)*Cornell University*, (2)*Massachusetts Institute of Technology*

Background: Non-speaking people with autism are not typically included in neuroscientific studies. Analysis of DVD-recorded sessions of non-speaking children with autism undergoing a communication therapy provides insight into the specific interactions between autistic behaviors and learning-related behaviors over time. Exploring learning-related behavior in children with autism will help to clarify the cognitive

processes involved in how non-speaking individuals with autism learn.
Objectives: The effects of communication therapy on learning-related behaviors and behaviors inhibiting the learning process in non-speaking children with autism were examined through a longitudinal analysis of video recordings.
Methods: DVD-recorded sessions of 8 children (6 boys, 2 girls, mean age 134.3 months, SD 42.8 months) undergoing a therapy that attempts to develop communication by a strategy of prompted pointing were coded, with special attention to identifying behaviors that were likely to impact learning in this non-speaking autistic population. Twenty-minute segments were coded from each of four sessions per child (the first, second, and fourth sessions, and, when available, the eighth session). An original coding scheme was developed to assess incidence and relative timing of prompts and choice complexity, as well as child behavior, including appropriate response, joint attention, reinforcement seeking, affect, and non-task activity. Antecedents for the coding scheme for autistic behaviors included the Early Social Communication Scales, the Autism Diagnostic Interview – Revised, and other published resources. The coding scheme for learning-related behaviors was based on the targeted behavioral objectives for the intervention.
Results: The effects of the therapy on joint-attention and other learning-related behaviors will be discussed. Preliminary data suggest that increased exposure to the intervention is associated with a decrease in non-task behaviors, with a correlated increase in joint attention to task-related stimuli.
Conclusions: Leaving aside the question of whether prompted pointing reliably evokes valid and independent communications, analysis of video-recorded sessions of non-speaking children with autism undergoing this therapy suggests that exposure to the therapy has a positive effect on joint attention and decreases time off task. These data can provide valuable insight into the specific relationships between autistic behaviors and learning-related behaviors over time.

128.122 122 Disruptions in Spontaneous Language in HFA: Indicators of Linguistic Processing Challenges. K. M. Belardi* and D. L. Williams, *Duquesne University*

Background: The language challenges of high-functioning older adolescents and adults with autism are difficult to assess. Few standardized language measures are available for this age/population and are primarily measures of narrow areas such as lexical knowledge. Samples of connected speech are generally analyzed for pragmatic features such as conversational turns. Narrative ability has been studied in children with HFA (Losh & Capps, 2003) but the focus has been on story grammar elements and grammatical complexity. Dollaghan and Campbell (1992) suggest the analysis of utterance *disruptions* during spontaneous language samples as a way to quantify speech production difficulties related to information-processing demands. This analysis may be useful for characterizing the language production of adults with HFA.

Objectives: To analyze spoken language samples of adolescents and adults with autism as compared to age and IQ-matched controls to determine if differences occur in measures considered to be indicators of problems with information processing.

Methods: Participants were 15- to 35-year old individuals with HFA (n=23) and typically developing controls matched for age and IQ, with Verbal IQs ³ 85. Autism diagnosis was established with the ADOS and ADI-R, and confirmed by expert clinical impression. A narrative language sample was collected using the "Create a Story" task from the ADOS. The language sample was transcribed using the Systematic Analysis of Language Transcripts (SALT) transcription format (Miller & Chapman, 2000). Measures of spontaneous speech including number of words, mean length of utterance (MLU), number of different words (TTR), number of mazes and abandoned utterances, and number of different word roots (NDWR) were computed using SALT-based analysis. Within-utterance "disruptions" were identified (based on the taxonomy of Dollaghan & Campbell, 1992) as an indicator of the individual's difficulty with language production.

Results: Samples have been transcribed for 23 older adolescents and adults with HFA. Transcript reliability was established (.99) with another graduate student. Language sample collection is ongoing for the matched control group. Initial analyses indicate a wide range of verbal fluency in this group with HFA. Total number of words produced ranged from 33 to 461 (Mean = 144.87; SD 92.62). The participants produced an average of 5.75 (SD 4.31) disruptions per 100 unmazed words (compared to an average of 5.31 (SD1.82)]

for Dollaghan & Campbell's group of 10 typically developing school age children). Four of the participants had clinically significant rates of disruptions (11.49, 11.51, 13.24, 18.09). Further analyses will be reported and comparisons will be made to an age and IQ-matched control group.

Conclusions: Some high-functioning individuals with autism have difficulty with the production of spoken language that may be related to information processing demands. These problems go beyond the diagnostically significant ones in pragmatic language. Measurement of disruptions during spontaneous speech production may be clinically useful for the characterizing the language production challenges of these individuals.

128.123 123 Language Profiles in ASD, SLI, and ADHD. H. M. Geurts*[1] and M. Embrechts[2], (1)*University of Amsterdam*, (2)*Dr Leo Kannerhuis*

Background: Developmental disorders might differ in their language profiles when using parent reports.

Objectives: In order to study language profiles with the Children's Communication Checklist-2 (CCC-2; Bishop, 2003) we carried out two studies.The first goal of the two presented studies was to explore whether there is a specific ASD language profile in terms of the nature and extent of their language skills and deficits and whether this profile depends on the age range. The second goal was to explore how this ASD language profile is related to the language profiles in other disorders such as ADHD and SLI.

Methods: In Study 1, children with ASD will be directly compared to children with ADHD and typically developing children (all aged 7 to 14 years). In Study 2, a direct comparison will be made between preschoolers with ASD, preschoolers with SLI and typically developping preschoolers (all aged 4 to 7 years).

Results: The first study indicated that school aged children with ASD have similar language profiles as children with ADHD. Both groups had relatively more difficulties with pragmatics than with structural language aspects. The second study indicated that both preschoolers with ASD and those with SLI show the opposite pattern, thus having relatively more difficulties with structural language aspects than with pragmatics. Finally, an increase in the presence of ADHD characteristics of impulsivity in these preschoolers is associated with an increase in language difficulties, while there is no such relation with inattention.

Conclusions: It seems useful to evaluate the communication abilities of children regularly in the course of development and take ADHD characteristics into account. Finally recommendations on clinical use of the CCC-2 are discussed.

128.124 124 The Use of Eye-Tracking to Investigate a Language-Specific Deficit in Intermodal Processing in Children with An Autism Spectrum Disorder. L. Hancock*, J. Bebko and K. Wells, *York University*

Background: Information from the environment reaches us over several modalities. For example, a dropped bowl is seen to break into many pieces and also heard to crash. Although information is received over different modalities, we perceive a unitary event. Newborn infants have been shown to integrate information reliably over two modalities. Spelke and Owsley (1979) have shown that 3½-month-old infants are able to associate the sound of their mother's voice with her face. The automatic integration of auditory and visual information is necessary for the development of speech and language. Impairment in communication is one of the characteristic deficits associated with autism (American Psychiatric Association, 1994). Individuals with autism often exhibit ineffective sensory processing, and integration of information across auditory and visual modes appears ineffective (Iarocci & McDonald, 2006). Deficits in this sensory processing may be related to some of the language impairments that characterize autism. However, efforts to replicate this language-specific deficit have yielded ambiguous results. Pilot testing presented at IMFAR in 2008 demonstrated that a modification of the experimental paradigm resulted in increased sensitivity and was appropriate for use in young children with an autism spectrum disorder. Objectives: The proposed study will investigate the language-specific deficit in auditory-visual intermodal processing of stimuli seen in children with autism. The study will attempt to ameliorate the ambiguity seen in previous research with the addition of eye-tracking and by utilizing a more sensitive paradigm. Methods: The current study used an adapted version of the preferential looking design for use with children with autism

and developmental disabilities aged 3-10. This involves displaying four videos on one screen, with an auditory track matched to only one of the videos. Intermodal perception (or the integration of the auditory and visual information) is considered to be present if the child shows a visual preference for the matched display. Videos contained either linguistic (person telling a story) or non-linguistic (person playing the drums or tap dancing) stimuli. Results: Eye movements were video recorded and analyzed using eye-tracking data based on the proportion of time spent looking in each of the four quadrants. Analysis is ongoing. Conclusions: A replication of previous results would corroborate and extend the notion of a language-specific deficit in intermodal processing in children with autism associated with their language difficulties.

128.125 125 Impact of Joint Attention Treatment on Children with Differing Language Abilities. K. A. Stickles*, T. Paparella and C. Kasari, *University of California, Los Angeles*

Background: Communication is the act of conveying information, meaning or content to another person through verbal or nonverbal behaviors (Stone & Caro-Martinez, 1990). Children with autism often display delays in developing and appropriately developing some of these communicative acts (Wetherby, Woods, Allen, Cleary, Dickinson & Lord, 2004). Objectives: The present study describes the effects of treatment on non-verbal communication skills for young children with autism during treatment. Participants in the study were in a randomized-controlled intervention study on joint attention skills with autism with two different treatment groups: joint attention skills treatment group or a comparison treatment group (play skills). The treatment phase lasted 5-6 weeks, on average (Kasari, Freeman, & Paparella, 2006). Methods: Fifty-two children participated in the study (39 boys, 13 girls). Each child was videotaped during a generalized play interaction with the therapist every third day of treatment. Each of the generalized play interactions was coded for the type of communicative act and the function of that communicative act. Two composite variables were used: *Total Joint Attention (JA) Composite* and *Total Behavior Regulation (BR) Composite*. *Total JA Composite* is the summation of the frequency of all the child-initiated joint attention skills (points, gives, shows, and coordinated joint looks). *Total BR Composite* is the summation of the frequency of all the child-initiated behavior regulation skills (reach, point, give, and coordinated joint look). Results: For joint attention skills, there was a significant effect of time ($F=7.96$, $p=0.001$), and a significant interaction between time and group ($F=6.13$, $p=0.03$). Participants were then split into two language groups (low- and high-language) based on receptive language ages from the Reynell Developmental Language Scales at program entry (Reynell, 1977). For the Joint Attention Group, the effect of Time was significant ($F=7.96$, $p=0.001$), but the effect of Language Group and the interaction of Time and Language Group were not significant. In the Play Group, neither the main effects nor the interaction effect were statistically significant.
Conclusions: This study revealed four main findings: 1) children randomized to the joint attention treatment increased their joint attention skills during treatment; 2) children in the joint attention condition also initiated more joint attention acts across the intervention than children in the play condition; 3) language (high or low) affected the change in joint attention skills during treatment for children in the play condition only; and 4) children with autism need to be taught joint attention skills, especially at low language ages, as joint attention skills not developing independently.

128.126 126 Referential Word Learning in Toddlers at Genetic Risk for Autism. T. Gliga*[1], M. Elsabbagh[2], K. Hudry[3], S. Chandler[4], T. Charman[3] and M. Johnson[2], (1)*Centre for Brain and Cognitive Development*, (2)*Birkbeck, University of London*, (3)*Institute of Education, University of London*, (4)*Institute of Education*

Background: Most theories of autism acknowledge the existence of a deficit in social cognition abilities, in individuals with autism or ASD. Nonetheless, the nature and the developmental origin of this deficit are still unclear. For example, the difficulties encountered by some young children with autism when acquiring language could stem from a specific impairment in social interaction (e.g. orienting to people for information and knowing how to make use of referential cues, like gaze direction) or from a more general attentional problem (e.g. being able to disengage attention from other salient environmental events and orient towards the referent of a word).

Objectives: The aim of the study was to examine referential word-learning abilities in a group of siblings of children diagnosed with ASD (Sibs-

ASD) and in a control group of 3-year-olds who have no family history of autism (Controls).

Methods: 30 children (15 Sibs-ASD and 15 Controls) were presented with video scenes containing an actress and two novel objects. The actress repeatedly labelled the least "interesting" of the objects. We used en eye-tracker to measure children's ability to disengage from the "interesting" object and follow the gaze of the experimenter towards the "boring" one. Children's success in the word-learning task was measured using a word-object matching test, in which they were asked to point to the referent of the newly learned word.

Results: Preliminary results show that both groups succeed in attaching the new word to its referent, despite the concurrent presence of another salient object. However, eye-tracking data revealed a number of individual differences in the distribution of eye gaze throughout the task, possibly suggesting differences in how success is achieved. These differences were observed, for example, in the amount of looking towards the "interesting" and "boring" objects. Sibs-ASD spent more time looking at the "interesting" but non-labeled object than at the labeled "boring" object. At the same time, Sibs-ASD looked longer at the actress when she was labelling the objects.

Conclusions: As a group, siblings of children with autism and controls show no difference in terms of their success in a word learning task, despite the high attentional load. Nonetheless, individual differences revealed different strategies employed to succeed in this task.

128.127 127 Does Bilingualism Affect Language Development in Young Children with Autism?. K. Leadbitter*[1], K. Hudry[2], K. Temple[3] and .. PACT Consortium[1], (1)*University of Manchester*, (2)*Institute of Education, University of London*, (3)*University of Newcastle*

Background: In children without developmental disabilities, bilingualism causes few long term difficulties and can bring about linguistic and cognitive benefits (e.g., Peal & Lambert, 1962). However, for children with language impairments, bilingualism in the family may act as an aggravating factor and further delay and complicate language development (e.g., Crutchley, Botting, & Conti-Ramsden, 1997). Autism often brings about severe delay and deviance in language development. To our knowledge, there have been no medium- or large-scale investigations into the effect of growing up within a bilingual home on the language development of children with autism. Parents often question whether they should use only one language with their child. Anecdotal evidence suggests that clinicians vary in their advice to families on this issue. It seems intuitive that restricting use to one language would maximise the child's language learning potential. However, this may have negative consequences for some families and may not be a realistic option for others. It may also be the case, particularly for more severely affected children, that bilingualism in the home makes little difference to language development over and above the effect of autism itself. It is also theoretically possible that children with autism, like typically developing children, are able to cope with and benefit from hearing more than one language.

Objectives: This study explores whether there is any evidence to suggest that growing up in a bilingual home affects the language development of preschool children with autism by comparing matched monolingual and bilingual children on standardised measures of receptive and expressive English language (the language of the country of residence).

Methods: A subsample of children from bilingual homes were identified from the baseline cohort of the Pre-school Autism Communication Trial (total N = 152; www.medicine.manchester.ac.uk/pact/). All children were aged between 2 and 5 years with 'core' autism. These children were individually matched with PACT children from monolingual homes on the following measures: chronological age, gender, autism severity (ADOS score) and socio-economic status. Comprehensive language assessments were made for each child upon entry to the study. These included: Preschool Language Scales (PLS), Vineland Adaptive Behaviour Scales Classroom Edition, and the McArthur Communicative Development Inventory (MCDI). Language assessments therefore came from three sources: parent, researcher and teacher.

Results: Preliminary analyses were performed on data from one of the three trial sites. These suggested that there is very little difference between children from bilingual homes (n = 10) and those from monolingual homes (n = 10) on receptive and expressive language measures (PLS and MCDI scores). The poster will present data

from the full sample to show whether these somewhat counter-intuitive preliminary findings are confirmed.

Conclusions: The results are discussed in terms of developmental theory, cultural considerations, and the implications for bilingual families and the professionals that advise and support them. The limitations of this research are highlighted, including the lack of information of competence in the non-English language and the likely confound of diagnostic processes. Wider issues surrounding the complexities of research in this area are raised.

128.128 128 How Early Do Parent Concerns about Development Predict Later Autism Diagnosis?. S. Ozonoff*[1], I. Cook[2], M. M. Hill[1], T. Hutman[3], S. J. Rogers[4], M. Sigman[3], M. B. Steinfeld[1], S. Macari[5] and G. S. Young[1], (1)*M.I.N.D. Institute, University of California at Davis Medical Center*, (2)*UC Davis*, (3)*University of California, Los Angeles*, (4)*M.I.N.D. Institute, University of California at Davis*, (5)*Yale University School of Medicine*

Background: Recently published guidelines from the American Academy of Pediatrics (AAP) recommend that pediatricians routinely ask parents about developmental concerns and screen all children for autism twice by the 2nd birthday. Parent concerns, along with other risks, can trigger a referral for specialized evaluation. Most previous studies have used retrospective parent report to examine how well early concerns predict later outcomes, but these can be biased by knowledge of the child's eventual diagnosis, poor recall, or lack of sensitivity to developmental differences.

Objectives: This study collected parent concerns about development for infants at high (n=136) and low risk (n=83) for autism, using a prospective longitudinal design, to see whether they were predictive of later autism diagnosis.

Methods: Parents were asked at intake and when their infant was 6, 12, and 18 months of age: "Do you have any concerns about [x's] development or behavior at this time?" Responses were recorded verbatim and coded by raters unaware of group membership. Concerns were grouped into two categories: ASD Concerns (specific concerns about social or communication development or repetitive behaviors, or general worries about recurrence of autism) and General Concerns (medical, regulatory, cognitive, behavior or other concerns). Participants were followed to 36 months of age, when they were classified into one of four outcome groups: Autism/ASD (n = 24), Other Clinical Outcomes (e.g., global developmental delays, speech-language delays, behavior problems; n = 45), High Risk Typical (no clinical diagnosis and had an older sibling with autism, n = 79), and Low Risk Typical (no clinical diagnosis and had older siblings without autism, n = 70).

Results: At intake, there were no differences in General Concerns between infants with and without an older sibling with autism, but there were significant differences in ASD Concerns (Wald $X^2 = 7.49$, $p < .01$; 19% high risk v. 1% low risk group). Change in rate of ASD Concerns from 6 to 18 months was also significantly related to outcome. Parents of the Autism/ASD outcome group had significantly more General Concerns across all ages (Wald $X^2 = 12.99$, $df = 1$, $p < .001$) and significantly more ASD Concerns at 12 and 18 months of age, as well as a steeper growth rate in number of concerns (Wald $X^2 = 9.55$, $p < .01$).

Conclusions: Not surprisingly, parents who already have a child with autism have more concerns about development of younger siblings than parents without a child with autism. At 6 months of age, these concerns do not predict which infants will go on to develop autism. By 12 and 18 months, however, parents of infants who are later diagnosed with autism have significantly more concerns, particularly in the areas of social and communication development, than parents of children with typical or non-autistic clinical outcomes. These results suggest that parent concerns about early development are good indicators of developmental problems and that the AAP guidelines to elicit and act upon parent concerns are valid.

128.129 129 Diagnostic Stability and Outcome of Toddlers with Significant Cognitive Delays and ASD Symptoms. H. Boorstein*, A. D. Verbalis, M. Barton, S. Hodgson and D. Fein, *University of Connecticut*

Background: As awareness of the importance of early detection of autism spectrum disorders (ASDs) has grown, diagnoses have been occurring younger and in children with more severe cognitive delays. However, it is not clear whether diagnoses made in young, significantly delayed children are stable and what their prognoses may be. In our Early Detection study, we do not

diagnose a child with an ASD if all mental age equivalents are under 12 months, but put them in a separate category, "ASD-low MA," since the diagnostic stability is unknown.

Objectives: To examine the diagnostic stability, prognosis, and characteristics of a cohort of children with significant developmental delays who were diagnosed with "ASD-low MA" at a young age.

Methods: Children received comprehensive evaluations at approximately ages 2 and 4 after screening positive on the M-CHAT. Twelve children (7% of the total sample of children with ASDs seen at both time points) had developmental levels below 12 months, as well as significant symptoms of an ASD, at initial evaluation. Autistic symptoms at both evaluations, as well as diagnosis at re-evaluation, were analyzed in this sample of children.

Results: The children, who were evaluated initially at a mean age of 25 months (SD=4.8, range=18.6-31.8), had mean nonverbal age equivalences of 8 months, as well as receptive and expressive language skills estimated at the 10 and 9 month level, respectively. Their mean CARS score was 35.6 and total scores on Module One of the ADOS (social plus communication) ranged from 11 to 21 (mean=17.7). They averaged 6.8 DSM-IV-TR symptoms of autism (range=3-9) and 10 of the 12 children displayed repetitive or stereotyped behaviors, which are typically less frequent in this age group. At re-evaluation (mean age=50 months; SD=4.8; range=41.8-57.7), all children continued to meet ASD criteria; 11 were diagnosed with Autistic Disorder and one remained classified as "ASD-low MA." Their mean nonverbal level was 20.3 months (SD=6.6, range= 11-33), with receptive language estimated at 16.1 months (SD=7.1; range=5-26) and expressive language at 15.7 months (SD=8.1; range=6-27); standard scores were all at floor level. The children's Vineland standard scores were all below 75, with the mean scores on all domains below 60. They continued to display significant symptoms of ASDs at re-evaluation; mean CARS score were 35.0, mean total ADOS (Module One) scores were 15, and the mean number of DSM-IV-TR symptoms was 6.7. At re-evaluation, all children displayed repetitive or stereotyped behaviors, most frequently stereotyped motor mannerisms (82% of the cohort).

Conclusions: Diagnostic and symptom stability was strikingly strong in this sample of young children presenting with severe developmental delays and symptoms of ASDs. All of the children met DSM-IV-TR criteria for Autistic Disorder as well as mental retardation when re-evaluated. It is notable that the majority of children displayed stereotyped behaviors from an early age and that all presented with them at re-evaluation. This study suggests that diagnoses of ASDs can be made reliably in young children with ASDs and significant developmental delays, with the prognosis poor in this subsample of children.

128.130 130 Intensive Behavioural Intervention for Preschool-Age Children with Autism Spectrum Disorders: Some Retrospective Analyses. L. Thorne*[1], D. Fazzio[2], C. T. Yu[1] and A. Cornick[2], (1)*University of Manitoba and St. Amant Centre*, (2)*St. Amant*

Background: Applied behavior analysis (ABA) is considered the most effective intervention for children with Autism. The ABA Preschool Program at St. Amant provides 31 hours per week of one-to-one intensive behavioral intervention and provides training for 5 hours of parent led intervention. The service is available for up to 3 years. The ABA team consists of a Consultant, Senior Tutor, and Tutors. Prior to the start of intervention, children are assessed on measures of adaptive, cognitive, language, motor skills, as well as autism characteristics and severity. All assessments are administered at intake and repeated each year the child is receiving services. The outcome data are used by the ABA Program to evaluate service outcomes on children's abilities.

Objectives: The objective of this research is to examine potential predictors of outcome after one year of intensive behavioral intervention.

Methods: We examined potential predictors of outcome for approximately 50 children. Specifically, we examined whether autism severity, age, early learning rate, and cognitive skills at intake are significant predictors of personal-social skills (Battelle Developmental Inventory), communication (Preschool Language Scale 4th Edition), maladaptive behaviors (Scales of Independent Behavior Revised), and skill acquisition (Assessment of Basic Learning and Language Skills, ABLLS) after one year of

intensive behavioral intervention.
Results: Multiple regressions reveal that language skills after one year were significantly predicted by age and cognitive skills at intake. In addition, skill acquisition after the first year of intensive behavioral intervention was significantly predicted by early learning rate at 6 months. None of the predictor variables significantly predicted personal-social skills or maladaptive behaviors.
Conclusions: The results are consistent with other studies that report an association between language skills and cognitive skills. In addition, other studies have suggested that age at intake also predicts outcomes.

128.131 131 Longitudinal Improvements in the Quality of Joint Attention in Toddlers with Autism. K. Lawton* and C. Kasari, *University of California, Los Angeles*

Background: Joint attention is a central deficit of autism (Mundy, Sigman, Ungerer, & Sherman, 1986; Loveland & Landry, 1986). Joint attention involves skills such as pointing to share, showing toys, and alternating gaze between people and objects. These skills are often accompanied by shared positive affect and vocalizations and generally within shared engagement with others (Kasari et al, 1990). Previous research suggests that the joint attention skills of children with autism may improve through early intervention (Kasari, Freeman, & Paparella, 2006), but accompanying shared positive affect and vocalizations are rarely described. Shared positive affect is important to joint attention because it may indicate the true nature of the communicative intent of the child (Bruner).
Objectives: To determine whether there was an increase in the quality of joint attention (shared positive affect, vocalizations) for children with autism who were randomized to a joint attention intervention, symbolic play intervention, or control group.
Methods: This study uses data from a previously conducted intervention (Kasari et al., 2006). The intervention randomized twenty preschoolers to a six-week joint attention intervention, sixteen preschoolers to a six-week symbolic play intervention, and sixteen preschoolers to a control group. The quality of joint attention was operationalized by the presence of the following constructs during a joint attention instance: spoken utterances, shared positive affect, or both spoken utterances and shared positive affect. Spoken utterances were defined as any utterance the child produced that was a phoneme or larger and shared positive affect was defined as a smile directed toward an adult.
The quality of joint attention was assessed during a non-verbal communication skill assessment, the Early Social Communication Scale (Mundy, 1995). This assessment was video recorded four times during the study: at entry, exit from the intervention, six months after exit, and twelve months after exit. Cohen's Kappa was.79 and was conducted on 20% of the assessments.
Results: This study compared the change in the quality of joint attention at all four time points. There were no significant between group differences on the constructs at entry, $p>.05$. There were main effects for group and time for spoken utterances during joint attention, positive affect during joint attention, as well as positive affect and spoken utterances during joint attention, $p<.05$. When follow-up contrasts were run, the joint attention and symbolic play group had significantly more instances of each joint attention type than the control group during the six and 12 month follow-ups, $p<.05$. Interestingly, the joint attention and symbolic play groups were not significantly different from one another at any time point, $p<.05$.
Conclusions:

At six and twelve months after the intervention concluded, children in the joint attention and symbolic play group had a higher quality of joint attention. Future research can investigate when exactly the quality of joint attention begins to improve and what factors may best predict the rate at which the quality of joint attention improves.

128.132 132 Clinical Description of Preschoolers with Pervasive Developmental Disorder Not Otherwise Specified. A. Snow*[1], L. Lecavalier[1] and C. Albright[2], (1)*Ohio State University*, (2)*Developmental Assessment Program, Nationwide Children's Hospital*

Background: The most frequently diagnosed pervasive developmental disorder (PDD) subtype is PDD-NOS, yet it is the least well characterized. Research on the boundaries between PDD-NOS and other PDD subtypes has been inconclusive. Studies that have compared different PDD subtypes in terms of external behavioral criteria have yielded discrepant results. Such inconclusive results may be due to unreliable diagnostic criteria, the failure to control for age and intellectual functioning, and the nature of contrast groups. Refining PDD-NOS is of significant

importance in understanding the etiology and management of PDDs.

Objectives: The purpose of the current study was to provide a clinical description of preschoolers with PDD-NOS. Profiles of adaptive and problem behavior were compared to those of youngsters with autism and other developmental disabilities (DD) with behavior profiles similar to PDDs.

Methods: Data were obtained at a tertiary autism diagnostic specialty clinic. Data continue to be collected at the time of this writing. A multidisciplinary team assessed the participants and diagnoses were confirmed using the ADOS. Participants were between the ages of 23-69 months (mean=42.4 months, SD=14.1 months). The sample included 124 preschoolers (n=65 DD, n=37 autism, n=22 PDD-NOS). Analyses were conducted on the entire sample and after individually matching children with PDD-NOS to those from the other groups on NVIQ, age, and gender (n=18 per group). Adaptive behavior was assessed with the Scales of Independent Behavior–Revised (SIB-R) and problem behaviors were assessed with parent and teacher versions of the Child Behavior Checklist (CBCL).

Results: Analyses on the entire group indicated that children with PDD-NOS did not differ from the other groups in terms of adaptive behavior. Parent CBCL ratings indicated that preschoolers with PDD-NOS scored significantly higher than the DD group on the PDD syndrome scale (p=.02), as well as on several items at p<.01: "avoids eye contact," "upset by new people or situations," and "too shy or timid." Teacher CBCL ratings indicated higher scores on only two items at p<.01: "disturbed by change in routine" and "strange behavior." When children were matched on NVIQ, age, and gender, groups did not differ from each other in terms of adaptive behavior or behavior problem domain scores. The only significant difference was that preschoolers with PDD-NOS scored significantly higher than preschoolers with DD on the item "disturbed by change in routine" (p=.007).

Conclusions: Data suggested few differences in adaptive and behavior problems between groups when controlling for level of functioning and age. The current study was the first to provide a clinical description of preschoolers with PDD-NOS by comparing them to diagnostically similar groups matched on level of functioning and age. Further studies should continue to investigate the impact of level of functioning on the nosology of PDDs.

128.133 133 The Effect of Teaching Attending to a Face on the Emergence of Joint Attention Behavior in Young Children with Autism Spectrum Disorders. T. Rovito Gomez*[1], I. L. Cohen[2] and L. McDonough[3], (1)*New York State Institute for Basic Research in Developmental Disabilities*, (2)*NYS Institute for Basic Research in Developmental Disabilities*, (3)*Brooklyn College, City University of New York*

Background: A failure to attend to the faces of others is the single best discriminator between 1-year-old children later diagnosed with an autism spectrum disorder (ASD) and those with typical development. A more advanced form of attending is referred to as joint attention, which is defined as behavior used in a social context to direct attention to an object or event, thus establishing a common focus of attention between a child, another individual, and an object of interest. A deficit in the development of joint attention skills is a defining feature of children diagnosed with an ASD and is clearly unique to the disorder
Objectives: The purpose of the study was to teach children with an ASD to attend to a face by training the participants to look at the face of the examiner with a stimulus that has been established as a reinforcer and increase the response by delivering the reinforcer contingent upon attending to the face of the examiner. Upon meeting mastery criteria, the participants were then required to follow the eyes and head turn of the examiner to the stimulus/reinforcer. Given the evidence that techniques for teaching attending to a face may have implications for joint attention behavior in individuals with an ASD, the present study is important if this behavior deficit is to be targeted in early intervention programs.
Methods: A single-subject, multiple-baseline-across-subjects experimental design was implemented to demonstrate experimental control for attending to face behavior. Three subjects between the ages of two to three years and diagnosed with an ASD using the ADOS-G participated. Single-subject research design demonstrates experimental control by introducing intervention progressively for each subject while *c*ontinuous assessment or observation of performance over time is measured.

Results: All three participants demonstrated an increase in the attending-to-a-face response and the following examiner gaze behavior as compared to baseline levels. An increase was also

demonstrated during generalization trials, which took place with two additional adults. The attending-to-a-face responses were maintained during post-training sessions for all three participants. In addition, anecdotal reports from parents indicated an increase in responses to joint attention bids outside of the training setting compared to pre-treatment levels.
Conclusions: Attending to the face of another provides the opportunity for episodes of attention sharing, which is crucial for the development of social behavior. If problems with these social behaviors are found in children diagnosed with an ASD, then there may be a deprivation of the necessary experience for the development of social behavior in autism beginning early in life because of a failure to attend to the faces of others. Should the face of another become a signal that certain responses will be reinforced following specific consequences, and because faces provide information related to social communication, further complex social behavior is more likely to occur as a result of the increased opportunities for reinforcement when attending to the face of another. Therefore, providing the environment that will significantly increase opportunities of positive experiences with faces for children with an ASD should be considered.

128.134 134 Concurrent Predictors of Receptive and Expressive Language in Toddlers on the Autism Spectrum. S. Ellis-Weismer*, M. A. Gernsbacher, C. Karasinski, C. Erickson, S. Stronach and H. Sindberg, *University of Wisconsin-Madison*

Background: There is a scarcity of information concerning the nature of early language development in children on the autism spectrum. With the exception of a recently published report by Luyster, Kadlec, Carter, and Tager-Flusberg (2008), most of the prior research with larger samples has been based solely on data obtained from a parent report measure of language. The purpose of the present study was to compare language abilities across multiple measures and to characterize predictors of early receptive and expressive language performance in a large sample of children within a restricted developmental age range.

Objectives: This study had two objectives. First, we examined the concurrent validity of three commonly used measures of early language development. Second, we explored predictors of current receptive and expressive language performance in a large sample of toddlers on the autism spectrum.

Methods: Participants comprised more than 100 toddlers (ages 23-39 months) on the autism spectrum. Diagnoses were determined using comprehensive diagnostic evaluations, including the ADI-R and ADOS. Language performance was determined using the McArthur-Bates Communicative Development Inventory: Words & Gestures (CDI), the Vineland-II Adaptive Behavior Scales (VABS-II) Communication subdomain, and the Preschool Language Scale (PLS-4).

Results: Pearson correlation coefficients indicated significant associations between receptive-receptive comparisons ($r=.65$ to $.73$, $p<.001$) and expressive-expressive comparisons ($r=.68$ to $.85$, $p<.001$) on the three different language measures. Stepwise multiple regression analyses were used to explore concurrent predictors of receptive and expressive language. Predictors entered into the regression models included maternal education, nonverbal cognition (as measured by nonverbal items on the Bayley Scales of Infant Development), scores on the Vineland-II Socialization and Fine Motor subdomain scales, and initiation and response to joint attention (as measured during a semi-structured play session with the examiner). For expressive language, the strongest concurrent predictor across all three language measures was the VABS-II Socialization subdomain scale. Some additional significant variance on the PLS-4 and VABS-II Communication subdomain was accounted for by Bayley nonverbal cognition scores and response to joint attention, respectively. For receptive language, scores on the VABS-II Socialization subdomain were also a strong predictor across all three language measures, as was Bayley nonverbal cognition. Less robust significant predictors consisted of response to joint attention and maternal education level. Initiation of joint attention and scores on the VABS-II Fine Motor subdomain were not significant concurrent predictors of receptive or expressive language scores on any of the three language measures.

Conclusions: Parent report measures (CDI and VABS-II Communication) and a clinician-administered test (PLS-4) yielded similar assessments of early language development in toddlers on the autism spectrum. VABS-II Socialization subdomain scores were a pivotal predictor of the ability to understand and use language for young children on the autism

spectrum. Bayley nonverbal cognition was primarily implicated in receptive, rather than expressive, language performance. Although response to joint attention played a minor predictive role in receptive (PLS-4) and expressive (VABS-II) language performance, it was not significantly associated with early lexical skills (CDI vocabulary understanding or use), as might have been expected.

128.135 135 Joint Attention, Play Behavior, and Language Abilities in Toddlers with ASD, Developmental Delay, and Typical Development. K. Burner*[1], J. Greenson[1], L. Elder[1], J. Lindsey[1] and G. Dawson[2], (1)*University of Washington*, (2)*Autism Speaks, UNC Chapel Hill*

Background: Joint attention abilities and play behavior are associated with language development in both typically developing children and children with ASD. Children with ASD are impaired in attending to faces and voices and responding to and initiating joint attention. These early social orienting deficits may represent one of the earliest indicators for ASD and contribute to later social, communicative, and language impairments. However, most of the research in this area has been conducted in the preschool age range. This study is one of the first studies to examine joint attention, play behavior, and language in toddlers with ASD. Objectives: To investigate the relationship between play, joint attention, language, and cognitive abilities in toddlers with ASD, developmental delay, and typical development. Methods: Participants included children 18-30 months of age with ASD (n = 58), developmental delay (n = 21), and typical development (n = 27). Toddler's play behavior, joint attention, cognitive, and language abilities were measured in all three groups using the Communication and Symbolic Behavior Scales (CSBS), Play Assessment Scale (PAS), Joint Orient, Preschool Language Scale-4, and Mullen Scales of Early Learning. Results: Preliminary results indicate significant group differences on measures of language ($F(2,100) = 152.95$, $p < .01$), joint attention ($F(2, 95) = 70.56$, $p < .01$), and play behavior ($F(2, 98) = 71.70$, $p < .01$). This pattern of results remained significant even when IQ was covaried. In the overall sample, joint attention ($b = .27$, $t(3.35)$, $p < .01$) and play behavior ($b = .48$, $t(5.80)$, $p < .01$) were significant predictors of concurrent language ability. However, when examining the ASD group alone, the relationship between joint attention and language ability was not significant. Conclusions: These preliminary data replicate findings of joint attention, play, and language deficits seen in young children with autism. One possibility in examining the lack of relationship between joint attention and language ability in the ASD group is due to low variability in the joint attention measure. Additional analyses will examine multiple measures of joint attention and play behaviors to clarify the relationship between joint attention, play, and language abilities in toddlers with ASD. It is important to examine the relationship between early communication, joint attention, and play skills since these may be useful targets for intervention. Future analysis of this sample will examine the development of these abilities longitudinally.

128.136 136 Microstructure of Saccadic Behavior in High and Low-Risk Infants: Visual Scanning of Static Novel Faces. J. T. Elison*[1], J. C. Chappell[1], A. Sabatino[1] and J. Piven[2], (1)*University of North Carolina at Chapel Hill*, (2)*University of North Carolina*

Background: Accessing and efficiently processing information from faces remains a compelling assay of social cognition in infancy. Previous research suggests that children and adults with autism use atypical face scanning strategies to acquire social information necessary to navigate complex social situations. Additionally, some research suggests that atypical face scanning strategies may be present in infants prior to a diagnosis and may represent an indicator of risk for an eventual diagnosis.

Objectives: As part of the IBIS Network investigating early brain development in infant siblings of children with autism at 6, 12, and 24 months, we designed an eye-tracking battery to assess basic cognitive and social-cognitive skills that may develop on an atypical trajectory in children that eventually meet diagnostic criteria for autism. One aspect of this battery is examining the saccade dynamics elicited when high- and low-risk infants visually scan unfamiliar faces. In addition to total time spent in specific areas of interest (AOI) such as the eye region and mouth region, we are particularly interested in the number of discreet fixations and the average duration of fixation in specified AOIs.

Methods: Eye-tracking data were collected via a Tobii 1750 eye-tracker. The face scanning task involves the presentation of static faces showing positive emotions for a short duration of time (4 seconds) in order to maximize scanning behavior

that represents an infant's strategy for acquiring salient aspects of a face encountered for the first time. In addition to measuring total gaze time, we extracted the number of discreet fixations and the average duration of fixation on specific AOIs. Associations between general cognitive functioning via the Mullen Early Learning Scales and markers of autism via the Autism Observation Scale for Infants (AOSI) will also be reported.

Results: Our current sample size [n = 12 high-risk sibs (9 six month-olds and 3 twelve month-olds), n = 7 low-risk sibs (6 six month-olds and 1 twelve month-old)] will nearly double over the next couple of months and we plan to present data from ~40 infants at IMFAR. Preliminary analyses indicate that that total scanning time of the face is equivalent for both groups (p = 0.925). There are also substantial individual differences in performance on the face scanning task in both groups, which will inform associations with the Mullen and AOSI as the n continues to increase. We will also accrue a number of follow-up assessments and data on ~20 children will be presented who have data at both 6 and 12 months of age.
Conclusions: As we follow these children longitudinally we expect to see patterns of specific deviations from the normal distribution that may lead to specific deficits as the children enter the second and third years of life. Additionally, we will be able to determine whether aspects of saccadic behavior and visual attention might serve as a compensatory mechanism that facilitates typical information processing strategies.

128.137 137 Measuring Treatment Outcome in Autism Preschools. A. Cariello*[1], J. Southwick[1], S. E. White[1], J. Dana[1], S. A. Baldwin[1], S. Stephens[2], C. Johnson[3] and M. South[1], (1)*Brigham Young University*, (2)*Giant Steps Preschool*, (3)*Wasatch Mental Health*

Background: As services for young children with autism become more widely available, there is a growing need for ready measures of treatment outcome. Such measures will demonstrate efficacy to stakeholders including funding agencies and parents, and can provide ongoing, targeted information to treatment providers regarding the progress of each child. A new treatment outcome measure, the Preschool Outcome Questionnaire (POQ), was recently shown to have good reliability and validity, and to be sensitive to change over time, when used in an intensive therapeutic preschool (Barker et al., in press). The POQ takes just a few minutes to complete for parents and/or treatment staff. The POQ is not specifically targeted towards measuring autism symptoms, rather it targets more general behavioral symptoms (including attention, motivation, social skills, and behavioral regulation) that are important for all preschool treatment programs. **Objectives:** This study evaluated the validity of the POQ with regard to an autism preschool population, and the ability of the POQ to detect change (behavioral improvement) on a monthly basis.

Methods: The Giant Steps Autism Preschool has three classrooms of twelve children each, divided according to symptom severity and level of functioning. The parents of 32 children agreed to participate in the study. Children were administered the ADOS at baseline. The POQ is a 35-item, 4-choice Likert scale focused mostly on overt behavior (e.g., "How often does/is your child resist being hugged" "Argue" "Have sleeping problems"). The POQ was administered on a monthly basis for 6 months, along with two other questionnaires that are relevant to behavior in children with autism but are not designed specifically to be sensitive to short-term change (the Social Communication Questionnaire and the BASC-2).

Results: Although the POQ and ADOS utilize different methods and focus on somewhat different behaviors, baseline POQ and ADOS scores demonstrated moderate correlations (>.6 for POQ and ADOS-Total; >.4 for POQ and ADOS-Social). We interpret this to mean that both instruments provide a window on the child's general functioning. POQ items demonstrated adequate internal consistency, and as expected captured more improvement in symptoms across the study period than either the SCQ or BASC-2. We discuss additional analyses of the mechanisms underlying the POQ (for example, evidence for stronger validity for the higher-functioning groups, and possibilities for the ideal time period between POQ administrations) and our ongoing efforts to identify a factor structure that fits the autism preschool population.

Conclusions: There is substantial ongoing discussion about the best ways to diagnose or identify autism in young children. This study takes a different tack, reporting on a new measure (the POQ) that tracks response to intensive preschool

treatment programs. This easy (5-10 minutes) measure can be administered frequently and data from each administration can be used to quickly target children who are not making expected progress. More work is needed, but the POQ offers tremendous promise for capturing treatment data for reporting to funding agencies and other important stakeholders.

128.138 138 Rapid Attention Shifting Deficits in Male Siblings of Autistic Probands. R. Hodges and A. J. Lincoln*, *Alliant International University*

Background: A disturbance in the ability to rapidly shift attention between auditory and visual modalities has been observed among individuals with known cerebellar damage and individuals with autism (AD). Based on the strong influence that genetics play in the presence of autism and the spectrum of abnormalities that first-degree relatives of individuals with autism show, it is possible that siblings of children with autism would also show structural changes in the brain, including the cerebellum, causing deficits in the ability to rapidly shift attention, but possibly to a lesser degree than the autistic proband.,
Objectives: The purpose of this study is to determine if siblings of individuals with autism also show this deficit in shifting attention, which could indicate that shifting attention could be an endophynotypic marker hey exhibit a phenotypic similarity to their sibling with autism and shift attention deficits are part of the broad autistic phenotype.
Methods: Participants included 20 individuals who have a first-degree sibling with a diagnosis of AD (SIB group) and 19 individuals with no known medical or psychiatric disorders who do not have any siblings with autism or other Pervasive Developmental Disorder (NC group).Individuals participated in two types of attentional tasks: focus attention and shifting attention. Five time bins, which indicate the length of time between the presentation of the cue and the target stimuli, were used to categorize responses. The time bins were as follows: 1) 0.4-2.49 seconds; 2) 2.5-4.49 seconds; 3) 4.5-6.49 seconds; 4) 6.5-10.49 seconds; and 5) 10.5 to greater than 30 seconds. There were two conditions, both of which required the participant to press a button on the joystick in response to a rare target. The two conditions included focus attention and shift attention. Within these two conditions there were two modalities- visual and auditory. In all conditions the participants were required to selectively attend to the designated stimulus modality, discriminate between targets and exhibit a simple motor response (button press) to the detected targets.
Results: The between subjects comparison (omnibus F) was non-significant, suggesting siblings of children with autism performed comparably to normal control subjects on the shifting attention tasks and there were no between-group differences. A planned comparison was performed, examining the response accuracy for the two groups (SIB and NC) in the shortest time bin of the shifting tasks. There was not a statistically significant difference between groups on either the visual shifting task ($F(1, 37) = 0.045$; $p = 0.834$) or the auditory shifting task ($F(1, 37) = 0.126$; $p = 0.724$). Interestingly, post-hoc analyses did suggest that males may demonstrate a shifting attention deficit. Cases were split into male and female. For the visual and auditory shifting tasks amongst the males only, p-values approached significance. These comparisons showed moderate effect sizes ($Eta^2=0.22$ and 0.25). This would have to be further assessed with a sample including more male participants.
Conclusions: Overall, results suggest that typically developing male sibilings of AD probands may show evidence of an endophyotype involving a reduced capacity to perform inter-modality rapid shifting of attention.

128.139 139 Correlation of Autism Traits in Families of Children with Autism Spectrum Disorders. R. Luyster*[1], E. Hanson[2], N. Coggins[3], M. Le[3], J. Lomibao[3], R. Travolta[3], B. Winklosky[3], E. Baroni[4], A. Cangialose[4], C. Davit[2], J. Doerr[4], A. Fong[4], K. Greenberg[4], R. Hundley[2], R. Iturralde[4], A. Johnston[4], A. Lian[4], A. O'Connor[4], M. Shahab[4], C. Tam[4] and S. L. Santangelo[1], (1)*Harvard Medical School*, (2)*Children's Hospital*, (3)*Massachusetts General Hospital*, (4)*Children's Hospital Boston*

Background: Prior research has indicated that autism spectrum disorder (ASD) is strongly heritable and that there are valuable lessons to be learned by studying family members of individuals with ASD. The Social Responsiveness Scale (SRS), developed by Constantino and colleagues (2000) is a quantitative measure of ASD traits. Constantino and Todd (2005) found intergenerational correlations of these traits (on the order of 0.4) between children and their parents, and between the parents themselves, in a non-clinical sample.

Objectives: It has yet to be determined if behavioral correlations between parents and between children and parents are also observed in a sample of families where at least one child has received a diagnosis of ASD. The present investigation is designed to address this question using a unique and comprehensively characterized sample that includes children with ASD as well as their unaffected siblings, mothers and fathers.

Methods: The three primary inclusion criteria for the current study were that families must (1) be biologically related, (2) live in the same household and (3) include at least one child who had received a diagnosis of an ASD (autism, pervasive developmental disorder-not otherwise specified or Asperger's disorder), confirmed by the ADOS and/or ADI-R. As of December 2008, sixty-seven families were included in the present sample, with a total of 163 participants. This was comprised of 45 mothers, 43 fathers, 50 affected probands (37 male, 13 female) and 25 unaffected siblings (12 male, 13 female). At the time of participation, parents ranged in age from 25 to 54 years (M=40.70 years) and children ranged in age from 3 to 24 years (M=7 years). Data characterizing autism traits were collected on all family members (mother report on father, father report on mother, mother report on children) via the SRS (Constantino et al., 2000), a questionnaire measure including 65 items and yielding raw scores between 0 and 195. The standardized version of the measure for children was used as well as a research version for adults (SRS-Adult Research Version; Constantino, 2005), and another for young children (SRS-Preschool Version; Constantino, 2006).

Results: The mean raw SRS score for mothers was 36.20 (SD=23.64), fathers M=32.40 (SD=25.36); unaffected siblings M=21.44 (SD=16.63) and probands M=96.92 (SD=32.90). Intraclass correlation coefficients were estimated on the following six pairings: mother-father, mother-proband, mother-unaffected sibling, father-proband, father-unaffected sibling and proband-unaffected sibling. Note that not all pairings were available for all families as not all questionnaires have been returned yet. We found significant correlations between mothers and fathers (n=39), ICC = .28 (p<.05) and between fathers and unaffected siblings (n=13), ICC = .45 (p<.05).

Conclusions: Even in this small preliminary sample, significant associations emerged between members of families of children with ASD. These findings indicate that – as has been reported in a non-clinical population – there may be intergenerational and assortative mating effects on ASD symptoms in unaffected family members of children with ASD. As this sample collection is ongoing and expanding, these findings will be updated with the addition of many more families over the upcoming months.

128.140 140 Parental History of Mood/Affective Disorders and Regression among Children with ASD: Results from AGRE Families. R. P. Goin-Kochel*, S. U. Peters and F. Scaglia, *Baylor College of Medicine*

Background: There is an abundance of literature supporting a preponderance of mood and affective disorders in the family histories of children with autism spectrum disorders (ASD; e.g., Bolton et al., 1998; Delong & Dwyer, 1988; Ghaziuddin & Greden, 1998; Lainhart & Folstein, 1994; Smalley et al., 1995; Zapella, 1996). However, it is not known whether a relationship exists between familial history of mood/affective disorders and regression in children with ASD. Some children with a history of developmental regression (e.g., those with cerebral folate deficiency, a subset of children with autism) have demonstrated abnormalities in folate metabolism that are corrected with folinic acid supplementation (James et al., 2004; Moretti et al., 2005). Interestingly, several reports also note (a) reduced folate levels among individuals with mood/affective disorders and (b) that folate supplementation in conjunction with pharmacological agents is superior to drug treatment alone in terms of facilitating clinical improvements in these individuals (e.g., Coppen & Bolander-Gouaille, 2005; Morris, Trivedi, & Rush, 2008). Thus, it seems plausible that parental history of mood/affective disorders could be a risk factor for developmental regression in ASD via an inherited disposition for abnormal folate metabolism.

Objectives: To examine (a) whether regression among children with ASD is more often associated with a parental history of mood/affective disorders and (b) whether children with the regressive endophenotype are different from children with autism who have not experienced regression in terms of level of functioning (i.e., IQ and adaptive behaviors).

Methods: Data were ascertained on the 361 families in the Autism Genetic Resource Exchange (AGRE) collection on whom parental medical history data is available. Phenotypic and demographic data of interest were downloaded from the AGRE website and imported into a SAS database. The proportion of parents with a mood/affective disorder was calculated using information in the medical history form. Loss (regression) items from the two different versions of the *Autism Diagnostic Interview-Revised* (ADI-R) were combined so that comparable/identical items were represented as one variable within the dataset.

Results: Preliminary analyses reveal a mood/affective disorder in one or both parents among 47.4% of this sample. Of the 748 children born to these parents, 35.0% experienced some form of regression, with 25.5% and 28.9% experiencing language loss or some other skill loss (i.e., social, play, self-help, motor, hand use), respectively. One-way ANOVA's indicate significant differences in level of functioning between children with ASD who have and have not regressed per the *Peabody Picture Vocabulary Test-III*, the *Ravens Colored Progressive Matrices*, and the *Vineland Adaptive Behavior Scales*. Chi-square and logistic regression analyses will be used to determine whether parental history of mood/affective disorder predicts a history of regression in these children.

Conclusions: Results are congruent with prior research on level of functioning among children with ASD who have/have not regressed. Next-step analyses will reveal whether parental history of mood/affective disorder is associated with regression in children with ASD and, if so, whether it increases or decreases risk for regression.

128.141 141 An Examination of the Relationship Between Parent and Child Pragmatic Language in ASD Families Using HLM. J. Varley*, R. Bernier and J. Munson, *University of Washington*

Background: Impairments in social or pragmatic aspects of language are hallmark features of ASD and differentiate individuals with ASD from those with other developmental disorders. Parents of children with ASD demonstrate more social communication difficulties than parents of children without ASD. This well-replicated phenomenon has been deemed the *broader autism phenotype*. However, relations between parent and proband's use of pragmatic language within the same family has yet to be examined.

Objectives: We analyzed the relationship between ASD parents' use of pragmatic language and the degree of pragmatic language impairment in their children. Various aspects of pragmatic language were assessed, including conversational skills, intonation patterns, gestures, and interest in social language. Clinician-rated as well as self-rated measures were analyzed for both parents and children. Relationships between Verbal IQ and pragmatic language were also assessed.

Methods: The sample consisted of 345 nuclear families containing at least two children with ASD. Data were available from 341 mothers, 294 fathers, 993 probands (n = 789 males and n = 204 females), and 128 unaffected siblings (n = 63 males and n = 65 females). All probands met criteria for an ASD according to ADI-R, ADOS, and clinical diagnosis. Pragmatic language in parents was obtained via items from the Broader Phenotype Autism Symptom Scale (BPASS; semi-structured clinical interview and observation), Social Competence Questionnaire (ComQ; self-report), and Family History Interview (FHI; semi-structured clinical interview). Pragmatic language in children was assessed using items from the ADOS (clinician observation), ADI-R (semi-structured clinical interview), ComQ (parent-report), and BPASS. Verbal IQ was measured in all participants with age appropriate Wechsler scales of intelligence.

Results: Random coefficient multilevel modeling was used to account for the nesting of individuals within family in the estimation of standard errors and parameter estimates. Specifically, random coefficient hierarchical linear models (HLM) were constructed to examine the relation between parent and child levels of pragmatic language in the variables of interest. All available data were used based on empirical Bayes estimation in HLM. Limited results are presented in this abstract. On the ComQ, mothers' likelihood of initiating a conversation with someone new significantly predicted child's likelihood of initiating a conversation, $t(261) = 2.15$, $p = 0.033$. Additionally, maternal Verbal IQ was significantly predictive of child's likelihood to maintain a conversation on the ComQ, $t(244) = 2.13$, $p = 0.034$. Both mother and father Verbal IQ predicted child Verbal IQ, $p < .001$ and $p <$

.01, respectively. However, in general, father's self-reported conversation skills and Verbal IQ were not predictive of child pragmatic language abilities.

Conclusions: Maternal pragmatic language abilities significantly predicted child level of pragmatic language level. Specifically, mothers with stronger pragmatic language skills had children with higher levels of pragmatic language. This same pattern was not found in fathers despite a strong relationship between father Verbal IQ and child Verbal IQ. These results support the possibility of a maternal transmission pattern in pragmatic language abilities in ASD.

Keynote Address Program
129 Copy Number Variations (CNVs) In Autism: What Do They Mean?

Speaker: S. W. Scherer*The Hospital for Sick Children*

129.00 Copy Number Variations (CNVs) In Autism: What Do They Mean?".

Invited Educational Symposium Program
130 Molecular Genetics of Autism

Organizer: J. Sutcliffe*Vanderbilt University*

Speakers: P. Levitt[1]M. W. State[2]N. C. Schanen[3](1)*Vanderbilt University*, (2)*Yale University School of Medicine*, (3)*Nemours*

Twin and family studies have consistently indicated a substantial genetic component to autism etiology. The last few years have witnessed significant advances in our understanding of the genetic architecture underlying risk for this condition. The emerging picture reveals a level of heterogeneity far beyond what was previously predicted. Evidence points to a mix of both common and rare variation at a large number of genes as being involved. The emergence of copy number variation (CNV) as a major risk category highlights the role of highly penetrant rare variation. Increasing observations of more discrete point mutations in specific candidate loci extend the spectrum of rare variants that contribute to the overall susceptibility landscape. It is very likely that some individual susceptibility genes will contain both rare variants and lower penetrance common alleles that confer modest increases in relative risk. In this session, we will review different examples of loci that exemplify the range of allelic architecture that is now apparent in the autism genetics field.

130.00 Introductory Remarks.

130.01 The Increasing Importance of Duplications of Chromosome 15q11.2-q13 in Autism Spectrum Disorders. N. C. Schanen*, *Nemours*

It is becoming increasingly apparent that segmental aneuploidy for the proximal long arm of chromosome 15 is a major etiologic contributor to autism (AUT) and autism spectrum disorders (ASD). The region is rich with large, complex low copy repeats (LCR) that facilitate a multitude of different deletions and duplications of typically stereotyped blocks of genomic material. The first copy number variants (CNV) of this region recognized in ASD were duplications, that primarily take two forms: interstitial duplications [int dup(15)] that lead to segmental trisomy for the involved genomic region and supernumerary isodicentric [idic (15)]chromosomes that lead to tetrasomy or mixed trisomy/tetrasomy. The critical region for this dup(15) phenotype overlaps the Prader Willi-Angelman Critical region and familial cases of interstitial duplications indicate that maternally derived duplication chromosomes that confer the autism risk. The dup(15) syndrome phenotype also variable cognitive impairment, hypotonia, subtle dysmorphic features and seizures. Despite the relative frequency of this diagnosis among the ASD population (1-3%), dup(15) syndrome often goes unrecognized in part because the dysmorphic features are subtle and behavioral/cognitive profile of the syndrome is not well defined. In 1999, we initiated a study of dup(15) in ASD, applying a combination of molecular and cytogenetic approaches to examine the duplication chromosomes and performing systematic cognitive and behavioral testing on a cohort individuals with confirmed duplications. These studies reveal an extremely high rate of AUT and ASD in this population, although notably, the phenotype is not fully penetrant. In addition, we find dramatic variation in overall function based on measures of cognition and adaptive behaviors. There appears to be a dosage effect on phenotype, with higher cognitive scores and adaptive function for individuals with interstitial duplications (trisomy) compared to those tetrasomy and hexasomy. Importantly, examination of gene expression in brain in two

individuals with idic(15) indicated that the level of gene expression did not equate to copy number and in one case, there was an apparent misregulation of paternally expressed genes in association with clinical features reminiscent of Prader Willi syndrome. In this educational session, I will provide an overview of the molecular and cytogenetics of the dup(15) syndromes, and describe the clinical and behavioral characteristics of syndrome based on a cross-sectional study of 64 cases of individuals with dup(15) syndrome who have undergone systematic assessment of cognition, autism diagnosis, and adaptive function. I will also briefly describe the recently identified chromosome 15q13.3 deletion syndrome

130.02 Role of Rare Genetic Variants in Autism. M. W. State*, *Yale University School of Medicine*

Multiple lines of evidence support the contribution of rare genetic variation to the etiology of Autism Spectrum Disorders: it has long been recognized that cytogenetic abnormalities are over-represented in affected children, there are increased risks for ASD in a substantial number of rare genetic syndromes, rare mutations have been either linked or convincingly associated with non-syndromic autism in a small number of cases, and recent data suggests an increased rate of large de novo copy number variations in simplex autism families. In the last several years, the genomic technologies available to investigate rare variation have advanced dramatically, offering multiple new opportunities to pursue studies in this area while at the same time highlighting key challenges confronting efforts to confirm the relationship between ASD and individually rare genetic events. This presentation will present the "rare-variant common-disease hypothesis" of complex genetic disorders, review the evidence for the involvement of rare variants in ASD, discuss recent findings from our laboratory regarding rare structural and sequence variations in the neuronally-expressed molecules Contactin 4 (CNTN4), Contactin Associated Protein 2 (*CNTNAP2*) and Contactin Associated Protein 4 (*CNTNAP4)* and present the rationale and study design for a large-scale, multi-site investigation of rare variation currently underway in the Simons Simplex Collection.

130.03 Enough May Be Enough - A Convergence of Genetic and Biological Evidence Identifying the MET Signaling Pathway as a Key Autism Risk Factor. P. Levitt* and D. B. Campbell, *Vanderbilt University*

Rapid progress is being made on a number of fronts with regard to understanding the etiologies that underlie the autisms. The autisms are among the most common of neurodevelopmental disorders, and are highly heterogeneous in disorder phenotype, longitudinal trajectory of symptoms and response to treatment. A brief overview of the current state of thinking regarding the genetic and environmental risk factors will be discussed. Work from our own laboratory will be the focus of the remainder of the lecture. The convergence of human genetics in autism and basic developmental neurobiology studies suggests that the MET receptor tyrosine kinase signaling is important for the proper assembly of forebrain circuits, particularly those involving cortical projection neurons in which MET is heavily expressed. Dysregulation of MET signaling leads to alterations in cellular morphology, synapse development, and functional disruptions in both model systems and in humans. Multiple, convergent human genetic data implicate this signaling pathway as a major risk factor for autism. First, our laboratory discovered that a single nucleotide polymorphism in the 5' regulatory region of the human *MET* gene is associated with autism. Second, there has been replication in 6 different family cohorts, plus identified copy number variants (CNVs) and rare mutations in the *MET* gene, and association with autism of two other genes in the MET signaling pathway. Third, certain single gene, syndromic disorders with high a prevalence of autism also involve this same cellular signaling pathway. Fourth, the MET promoter variant is functional, as it reduces gene transcription. Fifth, studies of human postmortem samples show that MET and other upstream molecules that regulate MET signaling are dysregulated in autism. A model of autism etiology will be presented in light of the basic and clinical research findings.

130.04 Obsessions On a Biomarker: Serotonin Genetics in Autism. J. Sutcliffe*, *Vanderbilt University*

The most persistent biomarker in autism is the phenomenon of elevated serotonin in ~30% of individuals with autism. This has been repeatedly observed and found to be a heritable trait. Because of this and other evidence, scientists have long speculated a role for serotonin in the genetic underpinnings of autism. Recent observations of rare serotonin transporter (SERT) mutations in autism families supports this "serotonin hypothesis". These mutations, also

found in families segregating Asperger syndrome, OCD and other neuropsychiatric phenotypes, result in a gain-of-function to SERT leading to elevated transporter activity. Other studies identified a common coding variant (Leu33Pro) in the integrin β3 gene (ITGB3) as influencing circulating serotonin levels and associating with autism risk. We now understand that ITGB3, which physically associates with SERT, alters SERT activity and regulation in an allele-specific manner and does so both peripherally and centrally. While SERT is a key player in regulation of serotonin signaling, it is only one node in a broader network of molecules that regulate serotonin. In this session, we will review findings from autism genetic studies that touch broadly on serotonin biology.

130.05 Discussion.

Oral Presentations Program
131 Neuropathology

131.00 Potential Contributions of Developmental and Epilepsy-Associated Neuropathological Changes to Sudden, Unexpected Death in Four People with Chromosome 15 Duplication and Autism. W. T. Brown*[1], T. Wisniewski[1], I. L. Cohen[2], E. London[1], M. J. Flory[1], I. Kuchna[1], K. Nowicki[1], J. Wegiel[1], S. Y. Ma[1], H. Imaki[1] and J. Wegiel[1], (1)*New York State Institute for Basic Research in Developmental Disabilities*, (2)*NYS Institute for Basic Research in Developmental Disabilities*

Background: The ~1% prevalence of epilepsy in the general population increases to ~33% in autism (Tuchman and Rapin, 2002). The interpretation of developmental changes in autism and in chromosome 15 duplication autism has been challenged by a need to separate lesions not associated with epilepsy from lesions that cause epilepsy or are produced by epilepsy (Sutula and Pitkanen, 2001). Epilepsy induces brain alterations that contribute to changes in circuitry, which potentiates seizure-genic foci (Armstrong 2005). Studies of epilepsy in non-autistic subjects have shown that epilepsy is associated with an elevation of APP expression (Shang et al., 1994) and diffuse nonfibrillar A beta plaque formation (Mackenzie et al., 1994, 1996). Defining the patterns of neuropathological changes caused by chromosome 15 duplications is in a very early stage, based on studies of only a few brains.

Objectives: Separation of developmental changes from those associated with epilepsy and those potentially increasing risk of sudden death.

Methods: Brains of four autistic subjects (11, 15, 20, and 25 years old) with chromosome 15 duplications, and four age-matched controls were examined by light microscopy including the unbiased morphometric method and immunocytochemistry, and by electron microscopy. Three affected subjects were previously diagnosed with epilepsy and all four died suddenly and unexpectedly.

Results: The study found reduced size of brain, and reduced volume of neurons and neuronal nuclei in the striatum, amygdala, entorhinal cortex and Purkinje cells, correspond to developmental abnormalities. Changes observed in two subjects, including hippocampal microdysgenesis with hyperconvolution and duplication of the granule cell layer in the dentate gyrus, would appear to be contributory to seizures and could be enhanced by seizures. Chaslin's gliosis, observed in one subject, and local neuronal loss may reflect epilepsy-related brain damage. Enhanced cytoplasmic accumulation of A beta protein in all four subjects may be a reflection of modified APP processing.

Conclusions: This neuropathological study of brains of four subjects with chromosome 15 duplications, showed developmental changes. In three subjects, changes associated with seizures and caused by seizures could have contributed to sudden death. However, central apnea, asphyxia and pulmonary oedema, as well as life threatening cardiac arrythmias during seizures (Earnest et al., 1992, Nashef et al., 1996, Reeves et al., 1996; Jallon 1997; Saussu et al., 1998, Thom et al., 1999) could not be excluded as a direct cause of sudden, unexpected
death.

Sponsors: Autism Speaks, the Department of Defense Autism Spectrum Disorders Research Program (AS073234), and the NYS Office of Mental Retardation and Developmental Disabilities. The Harvard Brain Tissue Resource Center (R24-MH 068855), and the Brain and Tissue Bank at the University of Maryland, Baltimore, provided tissue. The Autism Tissue Program coordinated tissue acquisition.

131.01 GABAergic and Serotonergic Receptor Alterations in the Fusiform Gyrus in Autism. A. Oblak*, T. Gibbs and G. Blatt, *Boston University School of Medicine*

Background: Autism is characterized by the presence of deficits in social interaction, language, and repetitive behaviors. A key to normal social functioning in humans is face processing, which enables individuals to identify others and understand the mental state of others. Recent imaging studies looking at the fusiform gyrus (FFG), the key area in face identification and processing, have been contradictory. Some studies have shown that patients with autism are capable of performing face perception tasks yet others have found the FFG and other cortical regions involved in face processing are hypoactive in individuals with autism. A recent stereological investigation has shown that there are fewer and smaller neurons in the FFG in autism. However, the neurochemical basis of this phenomenon is unknown. This study aimed to determine if an alteration at the receptor level could account for the contradictory findings in the imaging literature. We looked at two neurotransmitter systems that have frequently been implicated in autism, GABA and serotonin (5HT).

Objectives: To determine the density and laminar distribution of $GABA_B$ receptors, benzodiazepine binding sites, and $5HT_{1A}$ receptors in the FFG in adult autistic and control cases.

Methods: Single concentration receptor binding autoradiography experiments were completed in the FFG using ^{3}H-CGP54626 as a ligand for $GABA_B$ receptors, ^{3}H-flunitrazepam as a ligand for $GABA_A$ receptor benzodiazepine (BZD) binding sites, and ^{3}H-8OH-DPAT as a ligand for $5HT_{1A}$ receptors . Autistic (n=10) and control (n=10) brains were matched for age and post-mortem interval. Optical densities were measured in the superficial and deep layers using the Inquiry program. Data analysis was conducted using Student's t-test.

Results: $GABA_B$ receptor density and BZD binding site density were significantly decreased in the superficial layers (p=0.007; p=0.02, respectively) in autistic cases. In the deep layers there was a significant decrease (p=0.002) in the density of $GABA_B$ receptors in the deep layers, but no change in BZD binding site density. Additionally, there were significant reductions in the density of $5HT_{1A}$ receptors in both the superficial (p=0.02) and deep (p=0.04) layers in autistic cases.

Conclusions: A growing body of evidence suggests that individuals with autism have difficulties in face perception, implicating the FFG. Recognition of persons, and especially their individual faces, is a key part of an individual's social experience and successful functioning within a social group. This study demonstrates decreased receptor density in the superficial and deep layers of the FFG in two key neurotransmitter systems, GABA and serotonin, in autism. Abnormalities in the superficial layers suggest a disruption in cortiocortical connections, whereas abnormalities observed in the deep layers suggest altered efferent connectivity to sub-cortical regions. This study also provides important evidence regarding abnormalities in the GABAergic and serotonergic receptor systems, which may contribute to abnormal face processing in individuals with autism.

Acknowledgments: Human tissue was obtained from the Harvard Brain and Tissue Resource Center, The Autism Research Foundation, and the NICHD Brain and Tissue Bank for Developmental Disorders.

131.02 Emerging Patterns of Neuronal Growth Desynchronization in Autism. J. Wegiel*[1], I. Kuchna[1], K. Nowicki[1], J. Wegiel[1], S. Y. Ma[1], H. Imaki[1], T. Wisniewski[1], I. L. Cohen[2], E. London[1], M. J. Flory[1] and W. T. Brown[1], (1)*New York State Institute for Basic Research in Developmental Disabilities*, (2)*NYS Institute for Basic Research in Developmental Disabilities*

Background: Pathological acceleration of brain growth in the first year of life and deceleration in the second and third year appear to play a pivotal role in the onset of clinical signs of autism (Courchesne et al., 2001, 2003; Courchesne and Pierce, 2005). Distortions of brain development are reflected in abnormal neuronal development and cortical minicolumn organization (Casanova et al 2002, 2006), and local dysgenesis (Bauman and Kemper, 1995, 1996; Kemper and Bauman 1993, 1998).

Objectives: We hypothesize that the (a) acceleration and deceleration of brain growth is a reflection of developmental cellular pathology, (b) acceleration of brain growth results in production of immature and smaller than normal neurons, (c) deceleration of brain growth results in acceleration of growth of neurons, (d) desynchronization of the growth of neurons in the brain in early childhood may play a critical role in shaping the clinical manifestations of autism.

Methods: To characterize sequential age and brain-subdivision-specific patterns of neuronal growth, 11 major subdivisions of the brain in one brain hemisphere of 14 autistic and 14 control subjects 4 to 56 years of age were examined. Unbiased morphometric methods of estimation of brain structure were applied, including the Cavalieri method, fractionator, and nucleator (Microbrightfield).

Results: Early childhood (4 - 8 years) was the period of significant delay of neuronal growth in the majority of examined brain structures including four nuclei of the amygdala, three striatal subdivisions (caudate, putamen and nucleus accumbens), thalamus, entorhinal cortex, dentate nucleus and Purkinje cells. None or insignificant delay was observed in the cornu Ammonis sectors 1-4, lateral geniculate body, inferior olive and nucleus of facial nerve. Late childhood was the period of significant acceleration of neuronal growth compensating for an early childhood delay.

Conclusions: The presence of a similar developmental delay of neuronal growth in the majority of examined structures in early childhood may indicate that (a) the developmental delay of the growth of neurons is regulated in a similar way in many brain regions, and that (b) each component of these complex neuronal networks may have its own contribution to the clinical phenotype of autism. The absence of a significant delay of neuronal growth in other brain regions suggests desynchronization of mechanisms controlling the growth of neurons. We hypothesize that interactions of incorrectly developing neurons/networks with non-affected brain networks may still result in dysfunction of both, affected and non-affected networks.

131.03 BDNF-Akt-Bcl2 Anti-Apoptotic Signaling Pathway Is Compromised in the Brain of Autistic Children. X. Li*[1], A. Sheikh[1], A. Chauhan[1], V. Chauhan[1], C. X. Gong[1], F. Liu[1], W. T. Brown[2] and M. Malik[1], (1)*NYS Institute for Basic Research in Developmental Disabilities*, (2)*New York State Institute for Basic Research in Developmental Disabilities*

Background: It has been reported that many areas of the brain in autistic individuals show abnormalities including loss of pyramidal neurons and granule cells in the hippocampus, as well as significant loss and atrophy of Purkinje cells in the cerebellum. However, there is a paucity of neurochemical data paralleling these neurohistologic findings in the autistic brain. Emerging evidence points to apoptotic mechanisms being involved in certain neuropsychiatric disorders, including autism. However it is not known whether apoptosis is deregulated in the brain of autistic individuals.

Objectives: The aim of this study is to determine the roles of apoptotic gene p53 and anti-apoptotic gene Bcl2 in the autistic brain, as well as how the apoptosis related genes are regulated.

Methods: Frozen human brain tissue (frontal cerebral cortex) of 6 autistic patients and 6 age matched control subjects were obtained from the NICHD Brain and Tissue Bank for Developmental Disorders. Donors with autism fit the diagnostic criteria of the Diagnostic and Statistical Manual-IV, as confirmed by the Autism Diagnostic Interview-Revised. Participants were excluded from the study if they had a diagnosis of fragile X syndrome, epileptic seizures, obsessive–compulsive disorder, affective disorders, or any additional psychiatric or neurological diagnoses. This study was approved by the Institutional Review Board of the NY State Institute of Basic Research. In this study, Western Blot Analyses were used to detect the expression levels of Bcl2, Akt and Phospho-Akt (T308) in the brain homogenates. Immunohistochemistry studies were used to examine the expression of p53 in the brain sections. Enzyme-Linked Immuno Sorbent Assay (Elisa) was used to determine the concentration of brain-derived neurotrophic factor (BDNF) in the brain homogenates.

Results: Our studies show that Bcl2 is significantly down regulated, while the expression of p53 is increased in the brain of autistic children in comparison with age matched controls. We also found that the expression and phosphorylation/activation of Akt kinase that regulates Bcl2 are significantly decreased in the autistic brain. The down-regulation of Akt may result from decreased concentration of BDNF, the growth factor that modulates Akt activities

Conclusions: These results suggest that apoptosis may play an important role in the pathogenesis of autism and the compromised BDNF-Akt-Bcl2 anti-apoptotic signaling pathway could be one of the underlying

mechanisms responsible for the pathological changes in the autistic brain.

131.04 Increased Iba-1 Positive Microglial Cell Density and Somal Volume in the Autistic Dorsolateral Prefrontal Cortex. J. T. Morgan*, G. Chana, J. Buckwalter, E. Courchesne and I. P. Everall, *University of California, San Diego*

Background:

Autism is marked by early brain overgrowth; one brain region in which overgrowth is strongly pronounced is dorsolateral prefrontal cortex (DLPFC). Several studies have reported changes in gene and protein expression levels consistent with pro-inflammatory changes in the autistic brain. Qualitative observations and a non-significant trend increase in HLA-DR staining have suggested the possibility of microglial activation in the frontal cortex of adults and older children with autism.

Objectives:

Determine whether there are significant alterations in neuronal organization, local microglial-neuronal clustering, microglial density, and microglial volume in the DLPFC in autism using an antibody to ionized calcium binding adaptor molecule-1 (Iba-1), which images both activated and resting microglia. Assess whether alterations are present at the youngest ages, and whether there is any interaction with the presence of seizure.

Methods:

Tissue from the DLPFC of n=16 autistic and n=10 control hemispheres was sectioned at a thickness of 50 microns. Histology was performed in 8 gyri per case using the Iba-1 antibody at 1:1000 concentration with a hematoxylin-eosin counterstain. Density counts were performed for both gray and white matter via a 1.4 n.a. 100x objective using a 3-d optical disector with a 2 micron apical guard zone at sufficient sampling density to achieve a Schaeffer CE <.10 for each case. Volume was projected for all counted microglia from 2-d isotropic nucleator. Coordinate locations of microglia and neurons were collected at a high sulcal wall location over an area no less than 625 microns in width and extending from pial surface to white matter. A density-independent univariate spatial pattern analysis was performed on these coordinates, along with a bivariate spatial pattern analysis over a 35 micron range and a density-independent assessment of the average distance from microglia to their nearest neuronal neighbors.

Results:

Significant increases in microglial density were observed in autism in both gray (25%; $p<.001$) and white (17%; $p<.01$) matter. Significant increases in microglial volume were observed in autism in both gray (30%, $p=.04$) and white (43%, $p=.01$) matter. A significant increase in neuronal clustering was present ($p=.05$), along with an increase local microglial-neuronal clustering ($p=.01$) and decline in the microglial-neuronal nearest-neighbor distance ($p=.02$). In autistic subjects under 6 years of age (n=3), percent changes in microglial density and volume were remarkably similar to those observed in subjects over 6 years of age. The majority of microglial measures demonstrated greater alterations in the seizure-free autistic group than the seizure group. No consistent interaction with postmortem interval was observed.

Conclusions:

Increases in microglial density, microglial somal size, neuronal clustering, and local microglial-neuronal clustering are present in the DLPFC in autism and do not appear to primarily reflect effects of seizure or postmortem interval. The observed changes are reminiscent of inflammatory reactions in other disorders, but might also reflect aberrant microglial genesis or abnormal, non-inflammatory microglial activity in the developing autistic brain. The observation of microglial alterations in young autistic subjects that are similar to those in older subjects suggests that microglial abnormality may be one feature underlying early aberrant brain overgrowth.

131.05 Expression Profiling of TLR Signaling Pathway Genes in Brain Tissue from Patients with Autism. C. A. Pardo, A. Azhagiri*, C. Lawler and A. F. Zea-Vera, *Johns Hopkins University School of Medicine*

Background: The pathogenesis of autism has been associated with genetic and environmental factors that influence brain development and neuronal function. As part of the genetic and environmental interactions, immune factors and neuroimmune responses appear to play pathophysiological roles in autism. Innate immune mechanisms are involved in regulating

synaptic/dendritic organization as well as neuronal dysfunction. Neuroimmune responses such as microglial/astroglial activation are part of the spectrum of neurobiological abnormalities that occur in individuals with autism (Vargas et al 2005). Toll-like receptors (TLRs) and their signaling pathways are associated with initiation and regulation of the innate immune response to diverse pathogen-associated molecular challenges. At least 10 TLRs have been demonstrated in humans and some of them are expressed in neurons, astrocytes, and microglia in the central nervous system (CNS).

Objectives: To assess the role of TLR signaling pathways the brain of patients with autism and to examine the patterns of expression within the CNS.

Methods: Profiles of TLR signaling pathway gene expression was assessed by genomic techniques using PCR gene arrays. Brain tissues from 4 regions, midfrontal (MFG), midtemporal (MTG), anterior cingulate (ACG) and Occipital (OG) gyri from 7 patients with autism (age range 5-42 years, mean 14.6 years) and 10 control patients (age range 5-20 years, mean 12.8 years) were studied. Expression of selected TLRs was validated by immunoblot analysis. Cellular localization of TLRs in the CNS was assessed by immunocytochemistry and laser confocal microscopy.

Results: Although no significant statistical differences were observed in expression of TLR genes with the exception of TLR-2, the study revealed significant differences in at least 13 genes involved in TLR signaling pathways. The MFG and ACG regions revealed most of the changes in expression of TLR signaling genes. Most of the increases in gene expression occurred in the ACG, where genes such as TLR-2, IL-2, IRAK1, NFKB1 and TNFRSF1A, were significantly up-regulated ($p<0.05$). Interestingly, gene expression changes in the MFG showed down-regulation of different set of genes including SARM1 ($p=0.01$) and UBE2N ($p=0.01$). Immunocytochemical studies demonstrated that TLR-2 was localized in astrocytes and microglia cells, a pattern that was almost identical to TLR-3. The expression of TLR-4 was observed mostly in microglial cells.

Conclusions: The major focus of TLR signaling gene expression changes occurred in ACG, an area of important interest for social/behavioral changes in autism. The gene expression changes in ACG reflect the status of neuroimmune activation in selected regions of the cerebral cortex and concurs with previous observations of increased innate neuroimmune and neuroglia responses in autism. Two of the up-regulated genes, IL-2 and TLR-2, play roles in modulation of innate immunity and inflammation. The immunolocalization of TLR-2 in microglia and astrocytes support the view that TLR pathways are associated with neuroglia activation in patients with autism. Interestingly, two of the down-regulated genes in the MFG (SARM1 and UBE2N) are also associated with regulation of the number of neurons. This finding may suggests their involvement in neuropathological abnormalities such as the excess of neurons observed in some brain regions in autism.

Oral Presentations Program
132 Longitudinal Studies/Early Intervention

132.00 Developmental Trajectory in ASD and Broader Autism Phenotype in the First Three Years of Life. R. Landa*[1] and E. Stuart[2], (1)*Kennedy Krieger Institute*, (2)*Johns Hopkins Univ. School of Public Health*

Background: Autism is a heritable disorder; the genetic liability includes autism and milder developmental differences or impairments. Understanding developmental trajectory in the first three years of life of children at high risk for ASD will inform early detection efforts and research on neurobiological mechanisms of ASD.

Objectives: To define developmental trajectories associated with the Broader Autism Phenotype (BAP) and ASD from 6 to 36 months in younger siblings of children with autism.

Methods: A longitudinal, prospective design was used. Children were separated into groups based on an 'outcome' assessment at 36 months of age. The Non-Broader Autism Phenotype group (Non-BAP; n=140) did not meet outcome criteria for language or social delays or ASD (n=140). The Broader Autism Phenotype group (BAP, n=20) had an outcome diagnosis of language or social impairment (did not meet criteria for ASD). The ASD group (n=55) met outcome criteria for autism or Pervasive Developmental Disorder-Not Otherwise Specified. Dependent variables include standard (T) and raw scores from the Gross Motor, Fine Motor, Visual Reception, Receptive

Language, and Expressive Language scales of the Mullen Scales of Early Learning, and algorithm summary scores from the Autism Diagnostic Observation Schedule (ADOS). Mullen data were available at 6, 14, 28, 24, 30, and 36 months of age. ADOS data were available at all ages except 6 months. Analytic methods involved linear growth curve random effects models implemented using the R statistical software package. All participants gave informed consent for this IRB approved research protocol.

Results: No group differences were found for Mullen scores at 6 months of age. By 14 months of age, and for each subsequent age, the ASD group scored significantly lower on all Mullen scales than the Non-BAP group (p's=0.03 to <0.01). Language difficulties in the BAP group became more evident at age three, as increasingly complex linguistic skills were expected based on chronological age. Growth curve analyses showed that Mullen raw and standard scores decreased in the ASD group with increasing age ($p<0.01$, indicating slowing and, in some cases, regression). The qualitative social and communication abnormalities associated with autism were present in the ASD and BAP groups by 14 months ($p<0.01$). Growth curve analysis showed that ADOS scores for the Non-BAP and BAP groups remained stable with increasing age, but ADOS scores for the ASD group increased with age ($p<0.01$, indicating worsening).

Conclusions: Siblings of children with autism are at increased risk for altered patterns of development. Our data indicate that developmental slowing begins between 6 and 14 months of age for children with ASD outcomes, and persists through the third birthday. Social and communication symptoms of ASD, as well as repetitive behaviors and interests, appear by 14 months of age in siblings with 36-month diagnosis of BAP or ASD. There is a continuum of severity of expression of these symptoms, and they remain stable from 14 through 36 months for siblings with the BAP. Findings underscore the importance of developmental surveillance for younger siblings of children with autism.

132.01 Longitudinal Change in Symptom Domains by ASD Severity Trajectories. K. Gotham*[1], A. Pickles[2] and C. Lord[3], (1)*University of Michigan Autism & Communication Disorders Center (UMACC)*, (2)*University of Manchester*, (3)*University of Michigan*

Background: The Autism Diagnostic Observation Schedule (ADOS) is often a primary phenotype measure in research samples, though the modular format of this measure makes longitudinal data comparison difficult.

Objectives: To plot longitudinal trajectories of ASD severity among children and adolescents using standardized ADOS scores, then to examine raw total changes over time in ADOS Social Affect (SA) and Restricted Repetitive Behavior (RRB) domains within each trajectory class.

Methods: The standardized ADOS severity metric reported by Gotham, Pickles, & Lord (in press) was applied to 1026 cases of data collected longitudinally from 345 individuals referred for ASD. Standardized scores were fitted for latent classes of severity trajectories with and without covariates. Within each latent class, trends in Social Affect and Restricted, Repetitive Behavior raw totals as a function of age were described in order to examine contribution of each domain to overall severity patterns over time.

Results: A four class model of ASD severity trajectories best represented the observed data, including a persistent high severity class, a moderately severe class, and two classes that respectively increased or decreased in ASD severity over time. In the persistently high and moderately severe classes, average RRB scores remain approximately stable while SA scores appear to decrease slightly over time. Within the increasing and decreasing severity classes, both domains appear to increase or decrease respectively.

Conclusions: If replicated, identified classes of autism severity trajectory may help in making clinical prognoses and subtyping samples for neurobiological and genetic research. Insight into the direction, magnitude, and age periods associated with changes in ASD domain severity may be able to guide intervention efforts, as well as the study of developmental trajectory of these disorders.

132.02 Longitudinal Changes in Cognitive Ability in Male and Female Children with ASD. A. D. Verbalis*[1], H. Boorstein[1], J. Pandey[2], S. Hodgson[1], T. Dumont-Mathieu[1], M. Barton[1], J. Green[1] and D. Fein[1], (1)*University of Connecticut*, (2)*Children's Hospital of Philadelphia*

Background: Early studies suggested that female children with autism spectrum disorders

(ASD) exhibit lower overall cognitive functioning then male children with ASD. This hypothesis was challenged in a recent study, which found no overall difference in cognitive level between boys and girls in toddlers with ASD (Carter et. al., 2007). To explain this discrepancy, it is possible that previous studies missed a group of higher functioning girls with ASD, or that boys with ASD are more likely to show improvements in cognitive ability over time. Although longitudinal examination is warranted to determine the cause of this discrepancy in research findings, no study thus far has examined longitudinal changes in the expression of ASD symptoms or associated cognitive deficits, between boys and girls. Objectives: The current study examined changes in cognitive ability from 2 to 4 years of age in a group of children diagnosed with ASD. Methods: The participants in this study included young children who were evaluated twice after screening positive on the Modified Checklist for Autism in Toddlers (M-CHAT). Diagnostic stability was examined in 139 boys and 29 girls who received a diagnosis of ASD at one or both evaluations, at mean ages of 27 and 53 months. Further comparisons of cognitive ability were completed on 76 boys and 17 girls who maintained an ASD diagnosis and completed the Mullen Scales of Early Learning at both evaluations. Results: Broad diagnostic stability was similar for boys (84% maintained diagnosis) and girls (79% maintained diagnosis). Within the spectrum, female children were equally likely to be diagnosed with PDD NOS or Autistic Disorder (AD), while male children were more likely to receive an AD diagnosis at both evaluations. Repeated measures ANOVAs were completed on four of the Mullen subtests (Visual Reception, Fine Motor, Receptive Language, and Expressive Language) with test administration as a within-subjects factor and sex as a between-subjects factor. There were no significant interaction effects for any of the subtests. The Visual Reception, Receptive Language, and Expressive Language all showed a main effect for administration, such that both male and female children received higher t-scores at the second evaluation. These three subtests showed no main effect for sex. The Fine Motor subtest did not exhibit a main effect for administration, but revealed a trend (p=.07), suggesting that female children scored lower than male children. Follow-up chi square analyses indicated that there were no significant differences between male and female children, for any Mullen subtest, on the percent of children who stayed the same across the time points, decreased by more than 1 SD over time, or increased by more than 1 SD. Conclusions: These data indicate that female children with ASD exhibit a similar profile of change in cognitive abilities as male children with ASD. This finding supports the first theory indicated above and suggests that increased recognition of the symptoms of ASD has allowed higher functioning girls to be correctly diagnosed more often. These data are still preliminary and ongoing efforts are aimed at recruiting additional girls with ASD.

132.03 Long Term Stability of the Effects of Intensive ABA Intervention in Young Children with ASD in Italy. G. Doneddu[1], P. M. Peruzzi[1], G. Saba[1], L. Ferretti*[1], S. Marras[1] and R. Fadda[2], (1)*A.O.B. (Azienda Ospedaliera Brotzu)*, (2)*University of Cagliari*

Background: Children with Autism Spectrum Disorders (ASD) show dramatic improvements thanks to intensive and early Applied Behavior Analysis (ABA) intervention (Howlin, 1998). Despite the great deal of knowledge about early intervention programs in Autistic Spectrum Disorders, the longitudinal studies about the long term stabilities of intensive A.B.A. intervention in young children with autism in Italy are still rare. Objectives: This study was designed to evaluate the long term stability over 4 yrs of an ABA early intensive intervetion (ABA-int), an ABA non intensive intervention (ABA-non int) and an Eclectic intervention on the Vineland Adaptive Behavior Scale (VABS) scores and on the Leiter-R scores in ASDs in Italy. Methods: 45 participants with ASD (34 M; 11 F; aver.chron.age=7;8 yrs;ds:2;8; aver.IQ=69; DS=24), divided at the beginning of the study in three groups of intervention: ABA-int intervention group (10 hrs of DTT, 5 hrs of speech therapy a week); ABA-non int intervention group (5 hrs of DTT, 2 hrs of speech therapy a week); Eclectic intervention group. The participants were tested with the VABS and with the Leiter four times ones a year (t1 to t4). At the end of the study, all the participants got an ABA non-intensive intervention or an eclectic intervention. Results: The IQ scores increased significantly over the four yrs ($F=4,87;df=6;p<0,05$) in the ABA-int intervention group (t1= 53.7; t2=79,5; t3=86.7; t4=74.5) and in the ABA-non int intervention group (t1= 55.78; t2=62; t3=67,7; t4=64,4) but not in the

eclectic group (t1= 79.50; t2=72.50; t3=69.89; t4=69,33). Also the VABS scores increased significantly (F=2.6;df=3;p<0,05) in the ABA-int intervention group (t1= 1;4; t2=2;6; t3=3; t4=4) and in the ABA-non int intervention group (t1= 3;1; t2=4;5; t3=5;3; t4=4;6) but not in the eclectic intervention group (t1= 5;4; t2=5;11; t3=5;9; t4=4;3). Conclusions: The results highlight a robust long term effects of ABA-int early intervention in ASDs on IQ and on adaptive skills as well as an important effect of ABA-non int intervention on the same domains, supporting the efficacy of evidence based evaluation of these programs in Italy.

132.04 Outcomes of Community-Based Inclusion Programming for Toddlers with ASD. A. Stahmer*[1], N. Akshoomoff[2], A. B. Cunningham[2] and C. Vattuone[1], (1)*Rady Children's Hospital*, (2)*University of California, San Diego*

Background: While research suggests that children with autism benefit from inclusive programming, these types of intervention programs are rare and minimal research has examined outcomes for these programs. In a study of a community-based inclusion program for children 18- to 36-months of age, Stahmer and Ingersoll (2004) reported outcomes for a group of 20 children. The reported IQ gains were similar to those reported in research studies of young children with ASD in both intensive one-to-one treatment programs and inclusion programs. Both standardized and functional measures indicated significant gains.

Objectives: To examine the standardized cognitive, communicative, and adaptive outcomes, as well as functional communication and social outcomes of children attending a community toddler inclusion program using mixed methods of intervention and to examine predictors of positive outcomes.

Methods: The current study used a quasi-experimental design to analyze the outcomes of 93 young children with ASD in the same inclusive toddler program. Children were tested at entry and exit to the program using a battery of standardized assessments as well as functional checklists. Data for children enrolled in the program for at least 5 months (M = 8 months) were examined using analyses of variance. In addition, regression analyses were used to examine possible predictors of positive outcome.

Results: There were statistically significant increases from entry to exit in developmental quotient, adaptive behavior, expressive and receptive communication standard scores and significant decreases in disruptive behavior. Twenty-five percent of children exited the program with IQs in the typical range (>85) and another 30% in the borderline range (70-84). Examination of functional assessments indicated that at entry 30% of children had no communication skills, while only 9% had phrase speech and 8% were commenting. At exit, only 10% of children were not using language to communicate, 20% used single words, 30% had phrase speech and 25% were using commenting and other forms of reciprocal communication. At entry, 25% of children had no functional play, while only 2% were engaging in even simple forms of pretend play. At exit, over half of the children were engaging in pretend play. Approximately 50% of children exited the program with a diagnosis of autistic disorder and 36% exited with a diagnosis of PDD-NOS. A step-wise linear regression indicated that number of months in the program, and standardized expressive and receptive communication scores significantly predicted developmental level at exit.

Conclusions: Inclusion programming for toddlers with autism using a systematic combination of intervention strategies can lead to significant improvement in both standardized assessments and functional behaviors. Community agencies can successfully implement effective programming for toddlers with autism. Extended time in the program and early communication skills may be predictive of outcome.

132.05 Agreement Between Self-Report and Observational Measurement of the Use of Evidence-Based Practices in Community Early Intervention Programs for Children with Autism Spectrum Disorders. A. Stahmer*, S. Reed and C. Vattuone, *Rady Children's Hospital*

Background: Although a few specific treatment methods have been established as efficacious for some children with autism in laboratory settings, there has been little investigation of community implementation of interventions for children with autism. An examination of the use of community practices may assist researchers in facilitating knowledge transfer to practice settings.

Objectives: The goals of this study included (1) comparing provider report of strategy use to observed strategy use and (2) examining the relationship between community intervention and evidence-based practices (EBP) for ASD.

Methods: Seventeen providers serving preschoolers with ASD completed a telephone survey of techniques used in their programs and how they adapt these techniques in practice. Test/retest reliability was 90%. Providers were then videotaped in their classrooms for two hours per day across two days. Trained observers scored videos for activity type and intervention techniques used. Descriptive analyses examined provider use of EBPs and were used to determine agreement between self-report and observational data.

Results: Ninety-one percent of providers reported using at least one EBP in their program; however providers typically combined strategies (up to seven methods). Only 9% of providers chose techniques based on research evidence. All providers had concerns about limited training opportunities Agreement between self-report and observational data was poor. For example, 95% of providers reported using sensory integration strategies; however these methods only appeared in 5% of observations. Ninety-one percent of providers indicated using child choice as a teaching strategy, however this was observed in only 2% of observations.

Conclusions: These data highlight the importance of observational data in determining EBP use in community programs. The extensive use of eclectic models may be impacting the effectiveness of intervention by diluting the depth and structure of specific strategy use. Innovative methods of translation of EBP to community programs are needed to ensure effective implementation.

Oral Presentations Program
133 Emotion/Social Skills Intervention/Screening

133.00 What Is Wrong with Emotion Processing in Autism?. D. Williams*[1] and F. Happé[2], (1)*University College London*, (2)*Institute of Psychiatry, KCL*

Background:

Early experimental research suggested that children with autism have severe difficulties in recognising and experiencing all types of emotion (e.g., Hobson et al., 1988). More recently, it has been suggested that high-functioning individuals (with IQs over 70) have difficulties in recognising/experiencing so-called "social emotions" (e.g., embarrassment) only, but not "basic emotions" (e.g., happiness) (Heerey et al., 2003). However, recently even this assumption has been challenged. Hobson et al. (2006), for instance, found little evidence to suggest that children with autism fail to recognise the social emotions pride and guilt in experimental settings. Given that emotion processing deficits are thought to be core to autism (e.g., Lord et al., 1999), it is remarkable that experimental studies have not more uniformly discovered such deficits.

Objectives:

This study aimed to assess the ability of individuals with and without autism to:

(a) recognise, *in others*, expressions of "simple" emotions (happiness, sadness, fear), "complex" emotions (disappointment, surprise, disgust), and "self-conscious" emotions (pride, embarrassment, guilt), and; (b) report *their own* previous experiences of these emotions.

If experiencing and recognising social emotions is dependent on the same underlying psychological processes, and if these processes are impaired in autism, then recognition and reporting abilities should be correlated amongst comparison participants, but not participants with autism.

Methods:

Twenty-one individuals with autism and 21 age- and ability-matched developmentally disabled participants took part. For the recognition aspect of the study, participants watched nine silent, five-second video clips, each of an actor expressing a different emotion. Stimuli were taken from 'Mind Reading: An Interactive Guide to Emotions' (Baron-Cohen, 2004), which provided standardised expressions of each emotion. After each clip, the participant stated what emotion they believed was expressed by the actor.

For the self-report aspect of the study, participants were asked to define each of the nine emotions and to provide a description of a time in which they had experienced each. Self-reports of emotion experiences were rated on a scale of 0 to 2, according to their appropriateness and richness.

Results:

In line with predictions, amongst each group of participants, social emotions were significantly more difficult to describe in self and to recognise in others than either simple or complex emotions (all *p*s < .005, all *r*s > .42). Also, independent of age and verbal ability, the ability to report experiences of social emotions was correlated with the ability to recognise social emotions in others amongst participants with autism (r = .70, p = .003) and developmental disability (r = .47, p = .04). There were, however, no significant between-group differences in either emotion recognition or emotion reporting (all *p*s > .49, all *r*s < .13).

Conclusions:

These results might lead us to question the nature and/or severity of emotion processing deficits amongst people with autism. We will discuss the possibility that individuals with autism implement compensatory strategies to perform well in experimental settings despite atypical emotion-processing competence, noting however that this suggestion is contra-indicated in the current study by the similar correlations between recognising and reporting social emotions amongst each participant group.

133.01 Temperament as a Predictor of Variability in Adjustment among Higher Functioning Children with Autism. H. A. Henderson*[1], C. Schwartz[2], L. Mohapatra[1], N. Kojkowski[1], A. P. Inge[3], C. Hileman[1] and P. C. Mundy[4], (1)*University of Miami*, (2)*Yale University*, (3)*University of North Carolina at Chapel Hill*, (4)*UC Davis*

Background: Despite a common diagnosis, higher functioning children with autism (HFA) display great variability in emotional symptoms, personal adjustment and adaptive life outcomes. In the modifier model of High-Functioning Autism we propose that studying non-syndrome specific constructs, such as temperament, provides insight into this phenotypic variability. Temperament describes constitutionally-based individual differences in reactivity and self-regulation.
Objectives: In the current study, we examined the unique and combined influences of Surgency, the tendency to approach high intensity and novel situations, and Effortful Control, the ability to voluntarily regulate attention and inhibit or activate behavior as needed, on Internalizing and Externalizing Behavior Problems and measures of Adaptive Functioning.
Methods: Preliminary data are presented on thirty-six (30 male) children with HFA, ranging in age from 9 to 16 years (M=12.75 yr, SD=2.33 yr), who completed several self-report measures including the Early Adolescent Temperament Questionnaire (EATQ-R; Ellis & Rothbart, 2001), the Behavior Assessment System for Children (BASC-2; Reynolds & Kamphaus, 2002), and the Loneliness and Social Dissatisfaction Questionnaire (LSDQ, Asher & Wheeler, 1985). Parents completed the parent-report version of the BASC-2. The independent variables were *Surgency* and *Effortful Control* from the EATQ and the dependent variables were composite measures of *Internalizing Problems* (BASC SRP Internalizing Problems, BASC PRS Internalizing Problems), *Externalizing Problems* (BASC SRP Inattention/Hyeractivity; BASC PRS Externalizing Problems), *Personal Adjustment* (BASC SRP Personal Adjustment, BASC PRS Adaptive Skills), and *Loneliness* (LSDQ total). A series of hierarchical multiple regression analyses were conducted to examine the effects of Surgency, Effortful Control, and their interaction on each outcome.
Results: Internalizing problems were predicted by Surgency, β=-.42, p=.012; total R^2 = .17, and Externalizing problems were predicted by Surgency, β=-.37, p=.03 and Effortful Control, β=-.32, p=.05; total R^2 = .23. Personal Adjustment was predicted by Effortful Control, β= .46, p=.006, and the interaction of Surgency and Effortful Control, β=-.43, p=.02; total R^2 = .33. Similarly, the interaction of Surgency and Effortful Control predicted Loneliness, β= .50, p=.03; total R^2 = .37. Specifically, among children relatively low in Surgency, Effortful Control was positively associated with Personal Adjustment, $r(20)$=.66, p = .002 and inversely associated with Loneliness, $r(13)$ = -.59, p = .03. Among children relatively high in Surgency, however, the relations with Effortful Control were nonsignificant.
Conclusions: Surgency and Effortful Control appear to serve as protective factors against behavior problems among children with HFA. Low levels of Surgency and low levels of Effortful Control predicted particularly poor personal adjustment and high levels of loneliness. These findings nicely parallel findings isolating low levels of behavioral approach and effortful control as risk factors among infant siblings of children with autism and suggest that children with HFA who are low in Surgency may particularly benefit from interventions targeting self-regulatory skills. Results will be discussed in relation to an

emerging literature on the importance of basic motivational and self-regulatory processes in the modification of the expression of autism across childhood.

133.02 Evidence-Based Friendship Training for Adolescents with Autism Spectrum Disorders: Replication and Follow-up Study of the UCLA PEERS Program. E. Laugeson*, A. Gantman, A. R. Dillon, C. Mogil and F. Frankel, *UCLA Semel Institute for Neuroscience & Human Behavior*

Background:

Social deficits and poor friendship quality are common areas of impairment for youth with Autism Spectrum Disorders (ASD), yet the majority of social skills intervention studies for this population have focused on improving the social competence of younger children in the lower ranges of functioning. Few evidence-based social skills interventions exist aimed at improving friendships for higher functioning teens with ASD.

Objectives:

This study represents the second randomized controlled clinical trial of the UCLA PEERS Program, an evidence-based parent-assisted social skills intervention aimed at improving friendship skills among high-functioning middle school and high school adolescents with ASD. Treatment outcome, maintenance of treatment gains, and predictors of treatment success were examined.

Methods:

Twenty-eight participants and their parents were randomly assigned to a treatment with follow-up or delayed treatment control condition. Participants attended weekly 90-minute group sessions over a 14-week period. Targeted skills included: conversational skills; electronic communication; appropriate humor; developing friendship networks; peer entry and exiting skills; good host/guest behavior during get-togethers; good sportsmanship; changing bad reputations; and strategies for handling teasing, bullying, rumors/gossip, and arguments. Skills were taught through didactic instruction using concrete rules and steps of social etiquette in conjunction with role-playing exercises. Teens practiced newly learned skills during behavioral rehearsal exercises and parent-assisted weekly socialization homework assignments.

Results:

Outcome data reveal that, in comparison to a delayed treatment control condition, teens in the treatment condition significantly improved in their knowledge of social skills ($p < .0001$), showed an increase in teen-reported hosted get-togethers ($p < .05$) and parent-reported hosted get-togethers ($p < .05$), and demonstrated improvement in overall social skills ($p < .005$), according to parent reports on a standardized measure of social functioning (SSRS).

Data further suggests that treatment gains were maintained at a three-month follow-up assessment. Of the 12 participants with follow-up data, 58.3% reported increases in get-togethers maintained at follow-up ($p < .05$). Correlations between teen and parent reports were significant for hosted ($p < .05$) and invited get-togethers ($p < .01$).

Age and baseline parent reported social skills predicted treatment response. Mean age was 14.4 years ($SD = 0.5$) for responders and 15.8 years ($SD = 0.8$) for non-responders ($t_{11} = 3.49$, $p < .01$). Mean baseline social skills score was 42.0 ($SD = 7.4$) for responders and 32.0 ($SD = 5.2$) for non-responders ($t_{11} = 2.58$, $p < .05$). Other demographic variables including gender, ethnicity, school placement, IQ, and adaptive functioning did not predict treatment success.

Conclusions:

This study represents one of the largest of its kind in the treatment literature for adolescents with ASD. Findings suggest that the use of PEERS, a parent-assisted manualized social skills intervention, is efficacious in improving the social competence and friendship skills of teens with ASD. Treatment gains for hosted and invited get-togethers with friends were maintained at a three-month follow-up. Predictors of treatment success include age and social skills ratings by parents at baseline.

133.03 Examining Predictors of Treatment Success In a Parent-Assisted Social Skills Training Program for Teens with Autism Spectrum Disorders: The UCLA PEERS Program. A. R. Dillon*, E. Laugeson, A. Gantman and F. Frankel, *UCLA Semel Institute for Neuroscience & Human Behavior*

Background: Social skills training has become a widely used treatment in assisting individuals

diagnosed with Autism Spectrum Disorders (ASD) effectively fit into their social environment. However, most social skills treatment research has focused on younger and lower functioning children with ASD, with very little research targeting higher functioning older adolescents on the spectrum. Among the few intervention studies conducted with this population, very little emphasis has been placed on examining the factors that predict treatment success for this highly underserved population. Objectives: This study examines the predictors of treatment success for the UCLA PEERS Program, a manualized evidence-based parent-assisted social skills intervention aimed at improving overall social skills and friendship quality among adolescents 13-17 years of age with high-functioning autism or Asperger's Disorder. Methods: 61 adolescent participants and their parents were randomly assigned to a treatment condition or a delayed treatment control condition. Participants attended weekly 90-minute group treatment sessions over a 12-14 week period. Targeted skills included: conversational skills; electronic communication; choosing appropriate friends; appropriate use of humor; peer entry and exiting skills; good host behavior during get-togethers; good sportsmanship; strategies for changing bad reputations; and strategies for handling rejection including teasing, bullying, arguments, and rumors/gossip. Skills were taught through didactic instruction using concrete rules and steps of social etiquette in conjunction with role-playing exercises. Teen participants practiced newly learned skills during behavioral rehearsal exercises within the group, and parent-assisted weekly socialization homework assignments outside of the group. Factors associated with treatment success were examined across both groups.
Results: Participants were divided into two groups, based upon whether they hosted more get-togethers with peers by the end of treatment. Of the 43 participants (70.4%) who hosted more get-togethers after treatment, significantly better quality of friendships were also reported (p <.05), as well as significantly more invitations for get-togethers from other teens (p <.025). Adolescents who improved, reported an average of 3.4 more hosted get-togethers per month following treatment (p <.025) and an average of 2 more invited get-togethers at the end of treatment (p <.025). Baseline socialization variables that appear to predict treatment success included lower scores on adolescent knowledge of social skills (p <.025), number of hosted get-togethers prior to the intervention (p <.05), and number of invited get-togethers prior to the intervention (p <.005). Statistical analysis further revealed that higher scores on autistic symptom traits at baseline predicted treatment success (p *<.05*). Other demographic variables including age, grade, gender, ethnicity, school placement, IQ, and adaptive functioning were not correlated with treatment outcome.
Conclusions: These findings suggest that predictors of treatment success in the UCLA PEERS Program are correlated with greater autistic symptomatology at baseline and poorer social skills. Participants who were more socially impaired at baseline and were experiencing greater autistic symptomatology were more likely to improve their frequency of hosted get-togethers following treatment. Additionally, participants who had better quality of friendships were more likely to host get-togethers and to be invited for get-togethers at a peer's house following the intervention.

133.04 The Collaborative Puzzle Game: An Interactive Activity for Fostering Collaboration in Children with Autism Spectrum Disorder. A. Battocchi*[1], G. Esposito[2], A. Ben-Sasson[3], E. Gal[3], F. Pianesi[1], P. Venuti[2] and P. L. Weiss[3], (1)*Fondazione Bruno Kessler*, (2)*University of Trento*, (3)*University of Haifa*

Background: During the last decades, experimental studies have assessed the utility of innovative technologies for people with Autism Spectrum Disorders (ASD). These studies have considered a variety of different devices and environments which have shown their effectiveness as a means for supporting and promoting social and interactional abilities in children with ASD. Children with ASD seem to be highly motivated by computer-based activities; focusing on a computer screen can help people with ASD to reduce distractions from unnecessary sensory stimuli; moreover, computers are free from social demands and can provide consistent stimuli and predictable responses.

Objectives: In this abstract we present the design and a first evaluation of the Collaborative Puzzle Game (CPG), an interactive technology-supported game designed for fostering collaboration in children with ASD. The CPG interface was inspired by cardboard jigsaw puzzles and was developed to run on the MERL DiamondTouch table, a horizontal interactive surface that supports the

collaboration of multiple users. As in regular puzzle games, the task requires assembling pictures starting with pieces that are spread over the table surface. In the CPG, digital pieces can be dragged over the surface by direct finger touch and the game/actions is enriched with visual and auditory feedback. The CPG features a set of interaction rules called Enforced Collaboration (EC): in order to be moved from their original position, puzzle pieces must be touched and dragged simultaneously by the two players. We hypothesized that EC can represent an interaction paradigm that would help foster collaboration between children.

Methods: Two studies were conducted to test the effect of EC on the interaction and collaboration of pairs of children playing with the CPG. In Study1, 70 boys with typical development (M = 9.7y) were tested with the purpose of creating a baseline for evaluation with children with ASD. In Study2, 16 boys diagnosed with ASD (M = 13.5y) were tested. Both studies included two experimental conditions: one where EC was active and the other where children could independently move puzzle pieces. The effect of EC was tested on a number of quantitative performance and interaction measures directly extracted from the system.

Results: EC was associated with a more complex interaction, as demonstrated by longer completion times and a higher number of moves required to complete the task for both experimental samples. EC had a positive effect on collaboration, which was reflected by an increased rate of simultaneous activity by the two players. In children with ASD, EC was also related to a higher number of moves reflecting the need for coordinating the activity and negotiating moves during the game.

Conclusions: The Collaborative Puzzle Game was developed with the aim of providing a playful activity that can help children with ASD to foster collaborative skills by taking advantage of the Enforced Collaboration interaction paradigm. The results show that Enforced Collaboration is related to a more complex interaction and that it appears to have a positive impact on measures reflecting collaboration.

133.05 Catching and Studying Autism Early: The 1-Year Well-Baby Check-up Approach. K. Pierce*[1], C. Carter[1], M. Weinfeld[1], J. Desmond[1], E. Courchesne[1], R. Hazin[1], R. Bjork[2] and N. Schork[3], (1)*University of California, San Diego*, (2)*Rady Children's Hospital*, (3)*Scripps Research Institute*

Background: Early developmental screening is essential, not only to initiate immediate treatment and improve outcome for children with an autism spectrum disorder (ASD), but to allow prospective research designs. Here we discuss pilot results of a new prospective method, called the "1-Year Well-Baby Check-Up Approach" (1Yr-CU) that is both simple and practical, and is initiated by pediatricians as part of their regular routine. Using this method, infants in the general population are screened and tracked in an unbiased fashion thus allowing for studies of both fundamental behavioral (e.g., exploration) and biological features (e.g., patterns of brain growth) of autism at 12 months of age. Importantly, because the screening tool used (i.e., the CSBS Infant-Toddler-Checklist, Wetherby and Prizant, 2002) was originally designed to detect communication delays and not autism per se, the early bio-behavioral phenotype of key contrast groups, namely developmental delay (DD) and language delay (LD), can be studied as well. Objectives: (1) To determine the percentage of infants detected via the 1-Yr CU that test positive for an ASD at an older age (i.e., 30-36 months) and the unique pattern of screen scores that may distinguish infants at-risk for an ASD from those at-risk for a LD or DD; (2) To determine the ease of implementation of this program as indexed by pediatricians; (3) To identify biological and behavioral features that may capture a unique signature of infants at risk for an ASD in contrast to those that are DD, LD, or typically developing. Methods: This large-scale project is currently ongoing. To date, eighty-five pediatricians have screened 7,655 babies using the CSBS at the 1-Year Well-Baby Check-Up. Infants who failed the screening form were referred to our laboratory for further testing that included widespread biological (e.g., MRI) and behavioral testing (e.g., interaction patterns with mother, environmental exploration). Typically developing infants were referred as well. ANOVAs and other statistical tests were used as a first order examination of group differences on selected measures. Within the next six months as more infants reach an age of final diagnosis, multivariate regression techniques will be used to examine the single as well as combined behavioral and biological features that may distinguish infants at-risk for an ASD from those at-risk for a DD or LD. Results: Preliminary analyses indicate that of the infants

that failed the screen at the 1-Yr CU, rates of ASD detected are generally consistent with published studies (Fombonne et al., 2005), taking into consideration that Asperger's, late onset and regression cases would not be expected to be detected at 12-months. Results also indicated that infants at-risk for an ASD have abnormal brain growth trajectories and display significantly different patterns of environmental exploration and interactions with caregivers. Additional analyses, such as multiple regression, will be performed to generate a "signature" of infants at-risk for an ASD. Conclusions: The 1-Yr CU Approach successfully detects a percentage of infants who will eventually manifest an ASD, is easily incorporated into pediatric practice, and allows for the ascertainment of behavioral and biological markers at 12-months.

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134.01 1 Are Standard Scores Higher on the New Vineland?. K. N. Hurd*[1], A. Perry[2] and H. E. Flanagan[1], (1)*York University*, (2)*Thistletown Regional Centre*

Background: Adaptive functioning is typically defined as how well individuals function in everyday life including functional communication, social skills, self-helps skills, and community skills. Assessment of adaptive behaviour is an integral aspect of the diagnosis of intellectual disability (together with cognitive level) and is very useful in assessments of children with autism as well (Filipek et al., 1999; Miriam Foundation, 2008; Perry et al., 2002). The Vineland Adaptive Behavior Scales (VABS; Sparrow, Balla, & Cicchetti, 1984) have been widely used as a developmentally-referenced adaptive behaviour measure since the first edition was published in 1984. The Vineland-II was published in 2005 (Sparrow, Cicchetti, & Balla, 2005). The second edition retained the essential structure of the original with domains of Communication, Daily Living Skills, Socialization, and Motor Skills, but added some items, changed the basal and ceiling procedures, and changed the scoring somewhat. Clinical experience and anecdotal reports suggest that the new Vineland-II is resulting in higher standard scores than it should, which may have implications for clinical practice as well as the interpretation of research results.

Objectives: The purpose of this study was to investigate empirically the hypothesis that the Vineland-II is resulting in higher standard scores than would be anticipated as compared to VABS scores.

Methods: While administering the Vineland-II for clinical purposes in a sample of children with autism, a ceiling of 6 rather than 4 is used and several additional questions are included which address questions not directly asked by the Vineland-II, but included on the VABS. Then scores can be derived for the original VABS as if it had been administered and the two sets of scores compared. Approximately 50 children have been assessed to date and the final sample is expected to be approximately 75. Children will be diagnosed with autism or PDD-NOS and range in age from 24 to 84 months.

Results: It is expected that raw scores and age equivalents scores will be highly correlated across the two measures but that standard scores will be less highly correlated. It is hypothesized that the standard scores from the Vineland-II will be significantly higher than those from the VABS. Further, the interrelationship of age equivalent and standard scores from the two versions will be explored in relation to cognitive level and severity of autism.

Conclusions: As a frequently used measure of adaptive behaviour, and considering the importance of adaptive functioning in diagnosis and treatment planning, this topic is of clinical importance. It will provide invaluable information for the interpretation of Vineland-II results in low to moderate functioning children with autism, which may have additional implications for funding and resource allocation.

134.02 2 Linking Low-Level Visual Processing Strategies to Higher-Level Processing Abnormalities in Autism Spectrum Conditions. C. A. Palmer*, K. Plaisted Grant and G. J. Davis, *University of Cambridge*

Background: There is a large literature on visual processing abnormalities in individuals with Autism Spectrum Conditions (ASC). Previous research addresses both general visual processing, and category-specific visual mechanisms. We have developed a comprehensive experimental design to investigate low-level visual processing and relate this to higher levels of cognition. The two areas of investigation in which we are concerned are spatial frequency analysis and face-specific visual processing mechanisms. Previous studies have suggested there is a high spatial frequency (HSF) bias in ASC in face identification tasks, contrary to a low spatial frequency (LSF) bias that

is characteristic of control participants (Deruelle et al., 2004). We aim to investigate whether an atypical spatial processing style occurs across all image categories, or is related to the social nature of target stimulus.

Objectives: To address how task-demands influence spatial frequency biases and whether individuals with ASC differ in their strategy under certain stimulus conditions.

Methods: Participants were presented with spatial frequency modified images of cars and faces (low and high-pass filtered images and hybrids of these) in an identification task. Experimental manipulations were made involving presentation time interval, nature of competition and orientation of image.

Results: At the time of writing, data-collection from ASC individuals is not complete. However, experiments have been run on control populations. Results indicated a time-dependence to spatial frequency strategy selection for car target images with LSFs biased under short conditions, but HSFs dominant in longer presentation duration. On the contrary, there was a LSF bias across all conditions with face targets. This LSF bias was reduced when the face stimuli were presented inverted.

Conclusions: A different pattern of spatial frequency preference is exhibited for face and car images in typically developing individuals. The perceptual dominance seems to be influenced not only by the physical properties of the target stimulus, but also by the higher-level interpretation of the image; this is suggested by a reduced LSF bias for inverted face stimuli. If atypical spatial frequency bias is a general characteristic of ASC one would expect this to be evident in result for both car and face images. However, if the abnormality is specific to face stimuli, one might expect differences confined to processing this image category.

134.03 3 Local Precedence with Intact Global-Level Processing and Superior Simple Auditory Stimuli Processing Abilities in Adolescents with Autism. Y. Xiang and L. Wang*, *Beijing Normal University*

Background: Previous studies (e.g. Mottron *et al*., 2000; Foxon *et al*., 2003) found local processing superority by employing absolute sound, chord and musical rhythm, but whether global processing is intact in persons with autism is still in debate.

Objectives: we used a hierarchical auditory stimuli to investigate the effects of interference and contigence in auditory stimulus sequence processing in persons with autism and their perceptual processing ability to simple auditory stimuli.

Methods: twenty-seven adolescents with autism (mean age = 12;8 years) and twenty-seven non-autistic adolescents participated in the study. The participants were matched on Chinese norms of Raven's Standard Progressive Matrices RSPM score, CA, gender and manual laterality. Materials were auditory stimulus sequence composed of three sine swept waves created by a software program. The participants were asked to detect if the stimuli were rising, press 'rising' key, and if they were falling, press 'falling' key. a) global level processing judgement; b) local level processing judgment, c) simple auditory stimuli judgement.

Results: In global processing task, no significant difference between the two groups was found in global processing, but local-to-global interference effect existed in autistic group. In local processing task, local precedence was found in autistic group, and global-to-local interference effect in both groups. In simple stimuli task, participants with autism showed better perceptual performance than the comparison group.

Conclusions: Adolescents with autism showed intact global processing and local precedence, and superior simple auditory stimuli perceptual ability in auditory processing. These results support the Enhanced Perceptual Functioning hypothesis in autism, which proposes an enhanced low-level processing ability, together with intact processing of static global information.

134.04 4 An Eye-Tracking Study: The Effect of Task on Visual Attention to Faces in Autism. S. F. Hannigen*[1], C. A. Best[1], K. Rump[1], N. J. Minshew[2] and M. S. Strauss[1], (1)*University of Pittsburgh*, (2)*University of Pittsburgh School of Medicine*

Background: Individuals with autism demonstrate impaired ability to interact in the social world, and researchers have hypothesized that deficits in face perception may contribute to general difficulties in social interaction. Indeed, it has been found that individuals with autism distribute their visual attention to faces in an atypical manner (Klin et

al, 2002; Pelphrey et al, 2002; Jones et al, 2008) and that atypical face processing predicts level of social impairment (Klin et al, 2002; Jones et al, 2008). Many studies have shown that compared to typically developing individuals those with autism display increased looking to the mouth and decreased looking to the eye region of the face. Questions remain as to whether the face viewing behavior of typical controls and individuals with autism varies by task.

Objectives: The current study investigates the effect of task demands on the face viewing strategy utilized by typically developing individuals and those with high functioning autism.

Methods: Participants were typically developing children and adults and those with high functioning autism. Each participant completed two tasks, an emotion recognition (ER) task and a gender identification (GI) task. In the ER task, participants viewed 80 stimuli of subtle emotional expressions. Participants selected their answer from a forced choice list that followed each stimulus. Stimuli were created from Ekman photographs (Young et al., 2002); they exhibited angry, afraid, sad, and disgusted expressions. In the GI task, participants judged the gender of 72 randomly presented faces by pressing keys labeled man and woman. Eye-tracking data were collected to explore fixation length in two areas of interest: the eye region and the mouth region.

Results: Regardless of task, typically developing individuals spent more time looking at the eye region of the face than participants diagnosed with autism. Across tasks, individuals with autism spent more time than typical controls fixated on the mouth region than the eye region of the face. That being said, a significant interaction of task (ER task versus GI task) and diagnostic group (autism versus typical control) was found ($F=5.409$; $p=0.023$). During the GI task both groups spent a greater amount of looking time to the eye region of the face than they did during the ER task, however individuals with autism spent less time looking to the eyes than typical controls. During the ER task both groups spent more time viewing the mouth region of the face than they did during the GI task, but this effect was much more dramatic for the participants with autism.

Conclusions: While individuals with high functioning autism look more at the mouth and less at the eye region across tasks, it appears that their face viewing strategy does shift when asked to make judgments about different facial information. Like typically developing individuals, those with autism look more at the eye region when completing a GI task and more at the mouth region when completing an ER task. The difference lies in the degree to which individuals with autism attend to these regions.

134.05 5 Are Pictures Worth a Thousand Words? Testing the Validity and Reliability of the Pictorial Infant Communication Scale. A. Grivas Matejka*[1], T. Charman[2] and J. A. Burack[1], (1)*McGill University*, (2)*Institute of Education, University of London*

Background: The Pictorial Infant Communication Scale (PICS; Delgado, Mundy, Venezia & Block, 2003) is a brief (16-item) parent-report questionnaire designed to assess the nonverbal communication of infants and toddlers. To improve parental understanding of the specific behaviours being measured (e.g., joint attention), pictures are presented next to each item on the questionnaire depicting the behaviour.

Objectives: To assess the cross-time reliability and concurrent validity of two versions of the PICS, one with pictures (PICS) and one without pictures (NPICS), among typically developing children.

Methods: The participants included 70 typically developing infants and one of their parents at the time of enrollment into the study. The infants were randomly divided into two groups. The PICS with pictures was administered to one group (PICS group) and the PICS without pictures to the other group (NPICS group). The parents were asked to fill out the PICS when their child was about 12 and 18 months old. To obtain a direct clinical measure of the child's nonverbal social communication skills, the Early Social Communication Scale was completed when the child was about 12 and 18 months old. To obtain a parent-report measure of the child's language development, parents were asked to complete the short-form versions of the MacArthur Communication Development Inventory (MCDI) when the child was about 12, 18, and 24 months old. To obtain a direct clinical measure of the child's language development, the Mullen Scales of Early Learning- Expressive and Receptive Language Scales (MSEL-ERL) were completed at about 18 and 24 months old. Cross-sectional and

longitudinal correlations among scores on the PICS, MCDI, ESCS and MSEL-ERL were assessed for both groups.
Results: Cross-time reliability from 12 to 18 months ($r(30) = .45$, $p = .012$) was found for the PICS, but only marginally for the NPICS ($r(30) = .35$, $p = .056$).
At 12 months old the PICS Total, Initiating Joint Attention (IJA)and Initiating Behaviour Requests (IBR) scores were significantly positively correlated with ESCS IJA and IBR scores, but only the NPICS IJA scores were significantly positively correlated with ESCS IJA scores. Both the PICS and NPICS at 12 months were marginally positively correlated with MCDI scores.
At 18 months old both the PICS and the NPICS scores were marginally positively correlated with ESCS scores. The PICS RJA score was marginally positively correlated with MCDI scores and Mullen Receptive scores but not the NPICS.
With regard to longitudinal correlations, the PICS scores at 12 months were marginally positively correlated with MCDI and Mullen Receptive scores at 18 and 24 months old. The NPICS scores at 12 months were marginally positively correlation with MCDI scores only at 24 months old and Mullen Expressive scores at 18 and 24 months old.
Conclusions: Overall, both versions of the PICS show promising properties as a parent report measure to assess nonverbal communication among infants as young as 12 months old. The inclusion of pictures seems to improve parents reporting, especially at 12 months old. The examination of the PICS among infants at risk for autism would be beneficial.

134.06 6 Is There Any Early Developmental Factor That Verbal Acquisition Will Appear in Children with Autism?. J. Almeida*, R. L. Abreu, C. Café, S. Mouga, T. S. Miguel, C. Lobo, F. Duque and G. Oliveira, *Hospital Pediátrico de Coimbra*

Background: Autism (MIM 209850) is a complex neurodevelopmental disorder defined by impaired social interaction, communication and restricted, repetitive and stereotyped behaviour.
Whether there are differences in the early developmental abilities of children with autism spectrum disorder (ASD) and whether those differences in a specific period of time might predict verbal development, are questions of continued debate in autism research and that emerged from our clinical experience.

Objectives: Understand if there is any marker in the developmental/cognitive profile that can predict later verbal development.

Methods: The sample includes 34 subjects with autism based in Autism Diagnostic Interview Revised (ADI-R) and Childhood Autism Rating Scale (CARS) positive results. Inclusion criteria were two separated assessments with Griffiths Scale of Mental Development, the first at pre-school age and the second one at school age. All children benefited from speech-language therapy and proper teaching model based in the Treatment and Education of Autistic and related Communication Handicapped Children (TEACCH).
To find a marker in the developmental profile which can predict verbal development, Global Developmental Quotient (GDQ), Language Developmental Quotient (LDQ) and Performance Developmental Quotient (PDQ) were assessed at both periods. Later (at school age) we stratified the sample as nonverbal (NV) and verbal (V) according to the acquisition of language (spontaneous, flexible use of at least two words in combination, one of which must be a verb-ADI-R definition).
Statistic analysis (SPSS 15) was performed comparing the developmental profile of both subgroups with Mann-Whitney test for unpaired samples and Wilcoxon test in paired samples. Significance level (σ)=0.05.

Results: 34 subjects (26M/8F: 3/1) ADI-R positive and a median score CARS=35 (P_5 =30; P_{95}=50). At pre-school assessment (median age 49M) all children were NV and had a median GDQ=60. The group median LDQ was very low (40) and PDQ median value was higher (67), $g<0.001$. At the school period assessment (median age 81M) the median GDQ-65, and median PDQ-70 were similar to the first assessment, but the language development had increased significantly LDQ (40/52; $g=0.001$), as expected, since 17 of 34 children had become verbal.
We compared the developmental profile at preschool age between NV/V children. At the first evaluation both subgroups (NV/V) had low LDQ as expected (N/V=28; V=45), but they were very different in PDQ (NV=45; V=83; $g<0.001$). At the time of the second evaluation the verbal subgroup had a marked improvement in the LDQ=85 (first time=45; $g<0.001$), but the PDQ=95 (first time PDQ=83; $g=0.522$) remained equal. At the non verbal subgroup the results of LDQ (19) and PDQ (45) did not experience any change.

Conclusions: These findings demonstrate that in non verbal preschool children with autism, PDQ

may be an index that verbal acquisition will appear, regardless of educational intervention. These preliminary findings should be replicated in a larger sample.

134.07 7 Evaluation of Child and Treatment Variables Related to Communication Outcomes Using the Picture Exchange Communication System. J. Koudys[1], K. McFee*[1], J. Bebko[1] and A. Perry[2], (1)*York University*, (2)*Thistletown Regional Centre*

Background: As disordered communication is one of the core deficits of autism spectrum disorders (ASD), interventions logically focus on the development of functional communication systems. The acquisition of communication skills can have a considerable impact on the ability of individuals with ASD to participate in daily activities and build social relationships, as well as prevent the emergence of problem behaviour. One of the most frequently used approaches is the Picture Exchange Communication System (PECS). Based on the principles of Applied Behaviour Analysis, PECS users communicate by exchanging pictures of items with a communicative partner, often in exchange for preferred items or social interaction.

Research supports the use of PECS as a means of developing functional communication skills for individuals with ASD. However, less is known about the specific child and treatment variables associated with varying outcomes. Further, it is unclear whether skills such as picture discrimination or symbolic understanding of pictures, are prerequisite to teaching a behaviourally-based communication system like PECS.

Objectives: This study investigated the impact of teaching PECS to 22 individuals diagnosed with an ASD in a therapeutic summer camp program. Further, specific child and treatment factors related to different outcomes using PECS were explored.

Methods: Data were collected according to a pre-post longitudinal research design. Child variables and entry level of PECS were assessed at the beginning and PECS outcomes at the end of the 7-week summer camp. Treatment variables were tracked throughout.

Each child was assessed for developmental level and symptom severity at the beginning of camp using the Mullen Scales of Early Learning or Stanford Binet-5, Vineland Adaptive Behaviour Scales (2nd ed.), and Childhood Autism Rating Scale. Specific cognitive skills assessed included: discrimination among pictures, matching pictures and objects, learning associations between words and pictures, and the symbolic understanding of pictures. Treatment variables assessed included: fidelity (i.e., adherence to PECS protocol), intensity, (i.e., number of requests per day) and generalization factors (i.e., variety of reinforcers, activities, environments and people). Outcome variables assessed included level of PECS at the beginning and end of camp, vocabulary diversity, sophistication of communication, range of functions the system serves, as well as the types of environments and activities in which PECS was used.

Results: Data analysis is currently underway. Results will include a detailed description of child outcomes, along with analysis of the specific child and treatment variables associated with varying outcomes.

Conclusions: Given the prevalent use of PECS within the ASD population, the evidence base must be expanded to optimize treatment effectiveness. Implications for outcome expectancies and teaching will be shared.

134.08 8 Look at Mommy: Attention-Related Communication in Mothers of Children at Risk for Autism. K. Jakubowski* and J. M. Iverson, *University of Pittsburgh*

Background: When mothers interact with very young typically developing children, they simplify their speech and accompany it with a limited repertoire of concrete, informationally redundant gestures that reinforce attention to the verbal message (Iverson *et al*., 1999). Because Down Syndrome (DS) involves marked deficits in attention, this pattern of communicative modification is even enhanced in mothers who have a child with DS (Iverson *et al*. 2005). Given that attentional difficulties are also evident in children with autism (AD; Landry & Bryson, 2004), it stands to reason that mothers of children with AD may also modify child-directed communication to direct and maintain the child's attention and that this pattern could generalize to communication with later-born siblings of the child with AD (themselves at heightened risk, HR, for an AD diagnosis). To date, however, there is no research comparing child-directed communication of mothers with HR infants to that of mothers with low-risk infants (LR).

Objectives: Our aim was to: (1) examine and compare infant-directed communication produced by mothers of HR and LR infants; and (2) explore

the extent to which such communication is aimed at focusing or redirecting the child's attention.

Methods: Participants were 20 mothers of HR infants, 18 mothers of later-born LR infants, and their 18-month-old children. A 10-minute sample of maternal communication, obtained during a 45 minute, videotaped, naturalistic home observation, was transcribed verbatim, and all instances of child-directed maternal gesture (e.g., pointing, nodding head "yes"), action on objects (e.g., mother hands child a cup), and behavior on the child's body (e.g., tapping child's arm) were identified. Utterances were coded for (a) composition (i.e., speech only, mixed speech + gesture/action/behavior, gesture/action/behavior only); and (b) attention relatedness (i.e., focusing on or attempting to redirect the child's attentional state). Attention-related utterances were further classified according to whether they targeted the child's attention or the child's action.
Results: Mothers of HR infants produced approximately 50% fewer utterances than mothers of LR infants (M_{HR} = 104.6; M_{LR} = 163). For both groups, most utterances consisted of speech only (M_{HR} = .873; M_{LR} = .823). However, mothers of HR infants produced proportionately more than twice as many mixed utterances incorporating behaviors on the child's body (M = .127) and almost twice as many attention-directing utterances (M = .290) as mothers of LR infants (M = .056; M = .169 respectively). Finally, although the majority of attention-directing utterances for both groups focused on the child's action, mothers of HR infants were proportionately three times more likely to focus on the child's attention than mothers of LR infants (M_{HR} = .24; M_{LR} = .080).

Conclusions: Relative to mothers of LR infants, mothers of HR infants appear to be more sensitive to the child's attentional focus and more likely to play an active role in directing it. Having an older child with autism, in other words, may influence maternal behavior with later-born children, even when those children do not themselves necessarily manifest obvious autism symptomatology.

134.09 9 A Longitudinal Study of the Spontaneous Initiation of Vocal and Gestural Communication in Infants at Heightened Risk for Autism. B. M. Winder*[1], S. Poulos-Hopkins[1], M. V. Parladé[2], R. H. Wozniak[1] and J. M. Iverson[2], (1)*Bryn Mawr College*, (2)*University of Pittsburgh*

Background: Autism is characterized, among other things, by impairments in the spontaneous initiation of behavior, especially joint attention, symbolic play, and social communication.

Objectives: Because autism is generally not diagnosed before age two, our goal was to examine the spontaneous initiation of communicative behavior in infancy to assess its possible value for earlier identification. To maximize the likelihood that the sample would contain children eventually receiving an autism diagnosis and to evaluate the initiation of communicative behavior in infants at heightened risk for autism, we observed younger siblings of children already diagnosed with autism (High Risk Group, HR) and compared them to later-born infants with no such family history (Low-Risk Group, LR).
Methods: Fifteen HR and 15 LR infants were videotaped for 45 minutes at home in naturalistic interaction and semi-structured play with the caregiver at 13 and 18 months of age. At 36 months, HR infants were administered the ADOS-G. At that time, two children received a confirmed autism diagnosis. Videotapes were coded for spontaneous (i.e., production initiated by the infant rather than in direct response to adult communication) Vocalizations, Deictic Gestures (Request, Give, Show, Point), and Gesture/Vocalization combinations. Vocalizations were further divided into Words, Communicative Non-Word Vocalizations (occurring with eye contact or gesture to an interlocutor), and Non-Communicative Non-Word Vocalizations (no interlocutor present or no concomitant eye contact/gesture).
Results: Rates (per 10 minutes) of spontaneous initiation of communication involving Words ($p<.001$), Communicative Non-Word Vocalizations ($p=.04$), Gesture/Vocalization combinations ($p<.001$), and Gives ($p<.001$) increased significantly from 13 to 18 months for both groups. At both ages and overall, rates of spontaneous communication by HR infants were significantly lower than those for LR infants for Words ($p=.02$), Communicative Non-Word Vocalizations ($p=.03$), Shows ($p=.001$), and Gesture/Vocalization combinations ($p=.001$). Finally, a significant Group effect for Points ($p=.05$) was qualified by a significant Group by Age interaction ($p=.028$) such that a small and non-significant group difference in rate of spontaneous Points at 13 months (LR = .186; HR = .148) had ballooned to a large and significant difference by 18 months (LR = .572; HR = .266). No other main or interaction effects were significant. Finally, even by 13 months the two HR infants later receiving an autism diagnosis stood

out. They produced no Words; but more tellingly, they also produced few spontaneous Communicative Non-Word Vocalizations, only a single spontaneous Deictic Gesture, and no Gesture/Vocalization Combinations. At 18 months they remained at or near the bottom of the distribution on all initiated communication variables.
Conclusions: Results are consistent with a growing literature indicating that the younger siblings of children with an autism diagnosis are generally at heightened risk for communicative delay. In addition, although more research is needed, results also suggest that even by 13 months, when it is generally too early to expect high rates of spontaneous Word or Point production, greatly reduced rates of initiation of Communicative Non-Word Vocalizations and Shows, both of which are characteristic of typically developing 13 month olds, may index an eventual autism diagnosis.

134.10 10 Conversation in High-Functioning Autism: An Investigation of Gaze and Prosody during Face-to-Face Interaction. A. Nadig*[1], K. Bosshart[1], H. Shaw[1] and S. Ozonoff[2], (1)*McGill University*, (2)*M.I.N.D. Institute, University of California at Davis Medical Center*

Background: Conversation is an area of substantial difficulty for individuals with high functioning autism(HFA), although they have relatively unimpaired formal language. This may stem from the unstructured nature of face-to-face conversation, as well as its demands for the coordination of multiple modes of communication (e.g. eye gaze, prosody or intonation) along with speech. Previous studies investigated the social visual attention of adults and adolescents with HFA by tracking their eye movements as they watched social scenes unfold on video (Klinetal,2002; Norburyetal.,2008). These studies found reduced attention to actor's eyes in HFA, relative to matched comparison groups. The prosody or intonation patterns of individuals with autism have also been quantified, by conducting acoustic analyses on narratives produced by children and adolescents with autism (Diehletal.,in press). The pitch variation of HFA participants was found to be higher than that of comparisons, reflecting a sing-songy rather than monotone intonation.
Objectives: We carried out quantitative analyses of two modes of communication during face-to-face conversation, as they naturally occur in combination with verbal exchanges: eye gaze and prosody. This study aimed to increase our understanding of differences in both social visual attention and prosody in HFA, by sampling these behaviours "in vivo," as well as our understanding of the multiple modes involved in this fundamental forum of language use. Additionally, we compared these behaviours across two topics of conversation: generic vs. motivated.
Methods: Participants were children with HFA and typically-developing comparisons (TYP) matched on age (9 to 13 years), gender, language level, and PIQ. They participated in face-to-face conversations with an adult partner, on both a generic topic (siblings, pets), and a motivated topic (circumscribed interest or favourite hobby). We used eye-tracking technology to measure participants' visual attention to their partner's Face and Non-Partner regions (table, elsewhere) (n = 12 HFA, 11 TYP). For the prosody analysis audio files were extracted from video of the conversation, and 10 second samples were analyzed using PRAAT software (Boersma & Weenink, 2005) to measure pitch variation (n = 15 HFA, 13 TYP).
Results: Visual attention – There was a non-significant trend for participants with HFA to look less to their partner's Face overall than comparisons. However, visual attention to the Face was negatively correlated to autism severity (as provided by total ADOS-3 scores, r = -.74); participants with more severe autism symptoms looked less at their partner's face. Both the HFA and TYP groups looked significantly more to their partner's Face during the motivated topic of conversation than during the generic topic. Prosody -- Pitch variation was significantly higher in the HFA than the TYP group, corroborating the findings of Diehletal.(in press).
Conclusions: Multiple modes of communication contribute to differences observed during face-to-face conversation. We found prosodic differences between the HFA and comparison groups, and a trend for differences in visual attention, along with a strong correlation between autism severity and decreased attention to the partner's face. Interestingly, HFA participants, like comparisons, looked more at their partner's face during motivated, as opposed to generic, topics of conversation.

134.11 11 Parent Report of Social Communication Milestones in Very Young Children with Autism Spectrum Disorders. S. Shumway*[1], A. Thurm[1] and A. M. Wetherby[2], (1)*National Institute of Mental Health, National Institutes of Health*, (2)*Florida State University*

Background: Young children with autism spectrum disorders (ASD) have core social

communication deficits that impact gesture use. There is limited research on the specific gestures that may distinguish young children with ASD compared to matched control groups of both developmentally delayed and typically developing children, which would have important implications for earlier detection.

Objectives: The purpose of this study was to examine social communication profiles and use of gestures based on parent report for children diagnosed with autism (AUT), autism spectrum disorder (ASD), developmental delay (DD) in which autism was ruled out, and typical development (TD) from 18 to 36 months of age.

Methods: CSBS DP Caregiver Questionnaires (CSBS CQ; Wetherby & Prizant, 2002) were completed by parents of 176 children: 60 AUT (mean age=26.3 months), 23 ASD (mean age=25.3), 33 DD (mean age=24.9 months), and 60 TD (mean age=24.3 months). Participants were recruited from two sites, the NIMH and the FSU FIRST WORDS Project. The AUT, ASD, and DD groups were matched on nonverbal and verbal developmental level (developmental quotients) on the Mullen Scales of Early Learning (Mullen, 1995), and all groups were matched on chronological age. Scores were computed for the Social (emotion and eye gaze, communication, gestures), Speech (sounds, words), and Symbolic (understanding, play) composites.

Results: Children with AUT, ASD, and DD scored significantly lower than TD on all composites of the CSBS CQ using weighted raw scores. No significant differences were found between the AUT and ASD groups on the composite scores. In comparison to children with DD, AUT and ASD groups scored significantly lower on the Social composite only. Within the Social composite, children with AUT scored significantly lower than DD on all clusters: emotion and eye gaze, communication, and gestures. Children with ASD were significantly different from DD on gestures, but not emotion and eye gaze or communication. No differences were observed between AUT, ASD, and DD on the Speech or Symbolic composites.

Preliminary analyses on the 10 individual gestures measured on the CSBS CQ were conducted on a subset of the sample of children with AUT (n=29), DD (n=14), and TD (n=22). Compared to TD, significantly fewer children in the AUT group were reported to use all 10 gestures [all X^2's ≥ 4.4. All p values < .05]. Compared to children with DD, significantly fewer children in the AUT group were reported to use the following 5 gestures: showing, raising arms, waving, distal pointing, and nodding head [all X^2's ≥ 5.7. All p values < .05].

Conclusions: This study contributes to understanding the ontogeny of social communication milestones in children with ASD. The findings demonstrate distinct patterns of gesture use in young children with AUT compared to children with DD and TD. Preliminary analyses indicate that young children with autism have particular difficulty with certain gestures, particularly those often used for social initiation (showing, pointing, waving). These findings support the use of parent report of early gestures along with other social communication milestones for improving early detection of ASD .

134.12 12 Vocabulary in 2-Year-Olds with Autism Spectrum Disorder: a Magnified Verb Problem?. J. Parish-Morris*[1], R. Luyster[2], H. Tager-Flusberg[3], K. Hirsh-Pasek[1] and R. M. Golinkoff[4], (1)*Temple University*, (2)*Harvard Medical School*, (3)*Boston University School of Medicine*, (4)*University of Delaware*

Background:

Research suggests that verbs are harder for typically developing children (TDC) to learn than nouns (Gentner, 1982). Anecdotal evidence also suggests that children with autism spectrum disorders (CASD) have particular difficulty learning verbs. However, studies of early vocabulary composition in CASD are conspicuously absent from the literature. Exploring verb acquisition in this population is crucial because verbs are the gateway to grammar (Fernald, Perfors & Marchman, 2006). Verb referents are less perceptually available than words for concrete objects, which makes support from social and grammatical cues even more crucial to their acquisition, and may likewise place CASD at a learning disadvantage (Maguire et al., 2006; Parish-Morris et al., 2007).

Objectives:

What is the trajectory of verb acquisition in 2-year-olds with and without ASD? We hypothesized that because CASD experience limited access to the social and grammatical cues that scaffold verb learning, their lexicons would reflect a larger discrepancy in the proportion of nouns versus verbs than language-matched TDC.

Methods:

Vocabulary data for 24- to 30-month-old CASD with at least one word in their vocabularies according to parent report (mean age=27.41, N=75) was collected using the MacArthur Communicative Development Inventory Words and Gestures form (Dale & Fenson, 1996; possible nouns=184, possible verbs=55). A TDC group was constructed from a nationally normed sample (mean age=13.5, N=657) and matched to the CASD group on the number of nouns+verbs in the lexicon (M=83.78). Proportions (verbs/nouns+verbs) were calculated for CASD at 24 and 26-30 months, and for TDC groups using monthly norms from 11-16 months, which resulted in 12 sets of proportions (Dale & Fenson, 1996).

Results:

Preliminary analyses revealed that both groups had proportionately fewer verbs than nouns in their early lexicons, as expected (Bornstein et al., 2004; Swenson et al., 2007). Total number of nouns+verbs was highly correlated with age for TDC (r=.99, p<.001) but not for CASD (r=.31, p=n.s.). Using the complete CASD data set, we explored whether a verb discrepancy is most apparent in CASD with larger vocabularies. Results revealed a significant negative relationship between vocabulary size in CASD and verbs/verbs+nouns (r=.22, p<.05), suggesting that as the vocabularies of CASD get larger, the disparity between nouns and verbs grows (i.e., the proportion of verbs in the vocabulary decreases as total number of nouns+verbs increases). This relationship was not present in TDC (r=.46, p=n.s.; Tardif, 2006).

Conclusions:

This is the first study to demonstrate that 2-year-old CASD have more difficulty with verb acquisition than language-matched typically developing peers. Future studies will explore *why* the vocabulary composition of CASD differs from typically developing children. What characteristics differentiate CASD who acquire a cadre of verbs from those who do not, and what types of verbs are more readily learned? Research on verb acquisition in CASD has the potential to inform intervention, and will elucidate the specific mechanisms that underlie verb learning in both typically and atypically developing children.

134.13 13 Early Speech and Language Assessment in Toddlers with Autism. K. Stamper*[1], G. Dawson[2], N. Singh[3], J. Greenson[1] and M. Sharda[3], (1)*University of Washington*, (2)*Autism Speaks, UNC Chapel Hill*, (3)*National Brain Research Centre*

Background: Autism is a complex, pervasive developmental disorder with significant impairments in social and communication development as well as repetitive behaviors. There is evidence that early intensive behavioral intervention initiated at preschool age can result in substantial improvements in a large subset of children with autism, including significant gains in IQ, language, and educational placement. Early intervention has been shown to demonstrate gains for children with autism, but some children respond more to intervention than others. The factors that determine responsiveness to intervention are not well understood. However, some evidence suggests that early speech and language abilities are likely to be significant predictors of response to early intervention.

Objectives: *In this study, we examine a novel measure of speech production, referred to as "speech articulatory signatures," and its relation to other aspects of language ability in young children with ASD who are entering into a randomized clinical trial of early intervention. Such speech signatures, which reflect the maturation of fine motor control in speech, have been shown to follow a specific developmental time course in typically developing children (Singh L & Singh NC, 2008,* Developmental Science, 11*: 467-73).*

Methods: *The speech signature measure uses modern spectral analysis to investigate the development of articulatory and phonological features in vocal utterances: syllabic rhythm, format transition, and place of articulation. The current sample consists of 48 toddlers diagnosed with ASD (*M *CA = 23.48 mos.,* SD *= 3.92, range 18-30 mos., 37 M, 11F), as well as chronological age matched children with typical development, and chronological age and mental age matched children with idiopathic developmental delay. The children with ASD are participating in the NIMH-funded UW Early STAART study, which uses an approach that involves a relationship-based intervention framework to accomplish developmentally-based objectives using naturalistic application of applied behavior analytic principles in children diagnosed before 30*

months. Speech samples were gathered during diagnostic and other free play conditions video- and audio-taped for later analysis. Other measures available include the language subscales on the Mullen Scales of Early Learning and the Vineland Adaptive Behavior Scales, social orienting, and joint attention.

Results: *Initial spectral analyses of speech samples gathered in naturalistic conditions were found to yield reliable speech signature data in all three comparison groups.*

Conclusions: *Reliable measures of articulatory and phonological features of speech can be obtained from naturalistic speech samples taken in free play situations. Results of correlational analyses examining the association between characteristics of speech signatures and concurrent language ability will be reported. In addition, we will examine whether (1) toddlers with ASD differ from those with typical development and developmental delay in terms of their early speech signatures, and (2) whether, among the children with ASD, speech signature measures are correlated with other measures of language and social attention, all of which were assessed before entering the intervention study (Time 1). In the future, we plan to examine how the speech signature measure predicts response to treatment and whether it is a better predictor than standard measures of language.*

134.14 14 Building the Fundaments for the Future: The Development of Early Communication in the First Two Years of Life. K. T. Beuker*[1], N. N. J. Rommelse[2] and J. K. Buitelaar[1], (1)*Radboud University Nijmegen Medical Centre, Nijmegen Centre for Evidence-Based Practice*, (2)*Karakter Child and Adolescent Psychiatry University Center*

Background: Early communication forms the essential basis from which further cognitive and social development will take place. Major milestones in early communicative development are the emergence of joint attention and language. Joint attention is considered to provide the foundation of shared experience necessary for language acquisition. Early communication skills are commonly found to be impaired in Autism Spectrum Disorders (ASD).

Objectives: To obtain more fine grained information about the development of early communication skills and its individual differences in typical developing children. This may facilitate detecting a deviant pattern of early developmental skills in children with ASD.

Methods: In this current longitudinally study, the absence or presence of joint attention skills like sharing, following and directing attention and language skills were investigated as they emerged between 8 and 24 months of age in a single group of 23 typical developing infants. Data was collected during monthly home visits. First, the age and order of emergence for each specific joint attention skill were calculated. Next, the relation with language through cross-lagged correlations between joint attention skills at each month and the size of comprehensive and productive vocabulary at 8, 12, 18 and 24 months was tested. Last, the implications were investigated of an atypical developmental order of joint attention skills on language development.

Results: All joint attention skills emerged on average between the ages of 8 and 15 months. Based on the mean ages of emergences, the overall order of emergence was: Checking ☐ Sharing attention☐ Directing attention ☐ Following attention ☐ Directing attention with gaze alternation (g.a.) ☐ Following attention behind ☐ Referential language. The size of productive vocabulary at 8 months has a positive effect on the presence of directing attention (with g.a.) before the first birthday, but a negative relation in the period when joint attention skills are present in most children. Following attention within the visual field and direction attention with g.a. had an effect on comprehensive language throughout the second year of life. In the total sample, 18 children (78.3%) showed a typical pattern of development, in which checking, sharing, directing and following attention were found to emerge first before the emergence of directing attention with g.a. and following attention behind. The five children with an atypical pattern (with direction attention with g.a. earlier in the developmental sequence) had a larger productive vocabulary at 8 months compared to children with a typical development and an overall tendency to have larger receptive and productive vocabulary until 24 months.

Conclusions: The first two years of life represent a crucially important period in the emergence of early communication skills in which responsive joint attention skills tend to emerge before initiative joint attention. An atypical development does not per se have a negative effect on language, while results indicate that an atypical pattern could improve the size of vocabulary.

Though, these children showed a joint attention skill relatively early in development, children with ASD often have a delayed or absent joint attention development, which may result in diminished language skills.

134.15 15 Joint Attention of Children with Autism in Urban Early Childhood Center-Based Programs. C. Wong*, S. Booth and B. Gapinski, *Cleveland State University*

Background:

Young children with autism have specific deficits in joint attention, which is the ability to share interest about an object or event with another person. Because research has shown that joint attention skills are predictive of later language and social development, targeting joint attention is an especially important goal in early intervention. However, research in this area has primarily focused on children in suburban environments.

Objectives:

The aims of this study were to determine the extent children with autism in urban environments respond to and initiate joint attention behaviors in their everyday classroom environment and to explore differences in joint attention as related to demographic characteristics.

Methods:

In the study, children with autism from ten different early childhood special education urban classrooms were observed for approximately one hour over three separate days during structured and unstructured activities. Children were rated for joint attention skills from the Early Social Communication Scales (ESCS) and a videotaped play interaction with a caregiver. The children ranged in age from 40 to 73 months old and their mental ages ranged from 15 to 58 months. Most of the children were African American and lived only with their biological mother and siblings. The majority of mothers indicated completion of high school as their highest level of education and worked full time. Results were compared to a previously collected sample of children with autism from eleven different classrooms in a suburban environment using similar procedures as outlined above. In this suburban sample, children ranged in age from 38 to 62 months old and their mental ages ranged from 18.5 to 59 months. Most of the children were either Caucasian or Asian American and lived with both their biological mother and father. The majority of these mothers completed college but were not employed.

Results:

Preliminary results indicate no significant differences in joint attention between the children with autism in the urban environment and the children in the suburban environment. Although there was individual variation in the frequency and type of joint attention behaviors, overall, children with autism in both groups generally displayed few responses to and initiations of joint attention in the testing situation as well as in the classroom setting. Additionally, findings show that regardless of the environment (urban or suburban), the teachers seldom focused on joint attention in their teaching; when they did, it was rarely for the purposes of increasing joint attention skills.

Conclusions:

The preliminary results suggest regardless of demographic variables, the early core deficit of joint attention in young children with autism is the same. Therefore, while research findings describing joint attention characteristics of young children with autism from suburban environments may be generalized to children in urban environments, the effectiveness of interventions may still vary due to availability of resources. However, results do emphasize the importance of teachers in both urban and suburban environments targeting joint attention skills in their preschool special education classes for children with autism.

134.16 16 Relative Contributions of Speech and Gesture on the ADOS "Demonstration Task" in Adolescents with High-Functioning Autism. A. de Marchena* and I. M. Eigsti, *University of Connecticut*

Background: Gesture, as a form of nonverbal communication, is thought to be significantly impaired in autism spectrum disorders (ASD). Gestural impairments are considered in both the social and communicative domains of the DSM diagnostic criteria, and are assessed on multiple items of the ADOS and the ADI-R. Decreased frequency of gesture, as well as poor integration of gesture and speech, is considered more symptomatic. Despite the clinical significance of gesture in ASD, it has received scant empirical attention. As such, the origin of the gesture

impairment in ASD remains unknown. It is unclear whether gesture is specifically impaired or whether gesture impairments reflect the broader communicative impairment seen in ASD. Although early studies found reduced frequency of gestures in ASD, most studies find no group differences when controlling for the frequency of communicative acts.

Objectives: We investigate the formal qualities of co-speech gesture in high-functioning adolescents with ASD, focusing on 1) modality (gesture, speech or both) choice for event description and 2) gesture form. Gesture is an important communicative tool, and an understanding of how individuals with ASD gesture is a critical first step toward designing interventions to improve nonverbal communicative skills.

Methods: This study examines the spontaneous production of co-speech gestures in a sample of 12 high-functioning adolescents with ASD ages 13-17, compared with 12 chronological age-, gender-, and IQ-matched typically-developing (TD) adolescents (group differences, all F's < 2, all p's > .18). Participants were filmed during the demonstration task of the ADOS, in which they were asked to "show and tell" the experimenter how to brush her teeth. The speech and gestures used to describe four specific tooth-brushing events were coded, with a focus on errors in gesture formation (as in Dewey et al., 2007).

Results: Both groups encoded approximately the same number of events (ASD M = 2.6/4, TD M = 3.2/4) collapsed across modalities. Although most events were represented in both modalities (such that gesture complemented the information presented in speech), the TD adolescents had a bias toward representing these events as speech, whereas the ASD group had a bias toward representing these events as gesture (group by modality interaction, p = .06). Interestingly, no differences were found in the "structural quality" of gestures; that is, the gestures of the ASD group were all as well-formed as those of controls.

Conclusions: During a structured communication task, in which participants are explicitly instructed to "show and tell" the experimenter how to complete an often-enacted, familiar task, we find that high-functioning adolescents with ASD do not show a decreased frequency of gesture production relative to overall communication, nor do their gestures reflect motor planning difficulties. Rather, adolescents with ASD may rely more heavily on gesture to convey information, whereas TD adolescents may rely more heavily on speech. High-functioning adolescents with ASD may be more inclined to demonstrate familiar actions in gesture that are difficult for them to represent with words. Importantly, these adolescents were able to communicate information with gesture even when that information was absent from speech.

134.17 17 Production of Wh-Questions in Young Children with Autism. A. Goodwin*, D. Fein and L. Naigles, *University of Connecticut*

Background: Children with autism, by definition, show marked impairments in their language and communication skills. Asking and responding to questions is an important aspect of early social interactions. However, Wh-questions are especially impoverished in the language of children with autism. Previous studies have focused primarily on Wh-question use in experimental settings and across a wide age range. The current report examines the progression of Wh-questions by young children with autism in detail, making comparisons with typically-developing children matched on vocabulary. This research is part of a longitudinal study in which children are visited every four months across a 3-year time span to investigate the language development of young children with autism. This report includes production data from visits 2-4.

Objectives: We investigated the progression of various aspects of Wh-question production in 3-year-old children with autism, and vocabulary-matched typically developing children.

Methods: Mothers and children participated in 30-minute structured play sessions at each visit. At visit 2, the 10 typically developing toddlers (TYP: mean age = 24.68 months), and 10 children with autism (ASD: mean age = 35.40 months) were matched on expressive vocabulary (mean CDI scores = 375 and 369, respectively). Transcripts of the sessions were coded by (a) total number of Wh-questions, (b) number of different Wh-questions, (c) number of different Wh-words, (d) percent of total utterances that contained a Wh-question, and (e) percent of total utterances that were Wh-questions with a predicate.

Results: At visit 2, the ASD group produced fewer Wh-questions than the TYP group (Ms = 7.4 (TYP)

and 4.5 (ASD)). However, they did not differ in the number of different Wh-questions, number of different Wh-words, percent of total utterances that were Wh-questions, or the percent of total utterances that were Wh-questions with predicates. Between visits 2 and 3, the TYP group showed considerable increases in every category; for example, their number of different Wh-words increased from 1.7 to 2.6 and their percentage of total utterances that were Wh-questions with a predicate increased from 1.4 to 3.1, whereas the ASD group showed increases in number of Wh-questions (to 7.1) but not in measures (c-e). Furthermore, from visits 3 to 4, the TYP group continued to grow in Wh-question use and complexity whereas the ASD group showed little increase in Wh-question use. The TYP children also showed greater increases in expressive vocabulary between visits 2 and 3 (on average, a 150-word increase) than the ASD children did (on average, 50-word increase).

Conclusions: When matched to typical children on expressive vocabulary at visit 2, children with autism produce fewer Wh-questions, but otherwise show little difference in the types of Wh-questions that they use. However, the TYP group progressed dramatically in their use of Wh-questions between visits 2 and 3, while the ASD group showed little improvement across the time studied. This demonstrates that children with autism are not only delayed in the onset of Wh-question use, but also progress much more slowly. Further analyses will explore how much Wh-question growth is a function of general language growth.

134.18 18 Pretence in Children with High-Functioning Autism: How 'playful' Is Their Play?. J. M. Mifsud*[1], R. Kelly[1], C. Dissanayake[2] and S. R. Leekam[3], (1)*Olga Tennison Autism Research Centre*, (2)*La Trobe University*, (3)*University of Durham*

Background: Recent investigations into the symbolic play abilities of young children with and without autism have failed to show differences in their production of play (Dissanayake & Kelly, 2007; Dissanayake & Prescott, 2005; Hobson, Lee & Hobson, 2007). However, whilst the 'mechanics' of play are similar, Hobson et al. reported differences in children's level of playfulness, with the autism group showing less 'playful pretence' than the control children.

Objectives: The overall objective in this study was to replicate the findings of Hobson et al. (2007) in a sample of high-functioning children with autism, and to explore the associations between 'playful pretend' and the ability to engage in pretence, as assessed using the Test of Pretend Play (ToPP; Lewis & Boucher, 1997).

Based on the above findings, it was predicted that children with high-functioning autism (HFA) would show specific deficits in 'playful pretend,' despite their ability to engage in the mechanics of pretence.

Methods: The study utilised videotape footage of play sessions from a previous study of pretence (Dissanayake & Kelly, 2007). The sample comprised 20 children with HFA (16 male, 4 female) and 19 typically developing (TD) children (14 male, 5 female) aged between 4 years 0 months (48 months) and 7 years 5 months (89 months). The groups were matched on chronological age, verbal and overall mental age, performance IQ and full-scale IQ. A four-level rating scheme, adapted from Hobson et al. (2007) was used to code the level of 'playfulness' during administration of the ToPP, and during a 20-minute free play session. The aspects of playfulness rated were: investment in the symbolic meanings, self-awareness of the child as creating meaning, creativity, and fun.

Results: The 2 (Group) x 2 (Condition) ANOVA showed no effect of Group, $F(1,36) = .68$, $p > .05$, or Condition, $F(1,36) = .23$, $p > .05$, on the 'playful pretend' scores. After controlling for VIQ, 'playful pretend' was correlated with performance on the ToPP for both groups under the structured condition, but not during free play.

Conclusions: The children with HFA were just as playful and invested in play than the TD children under structured and free play conditions. These results fail to support the previous findings of Hobson et al. (2007). Children's ability to engage in pretence is more strongly associated with their degree of playfulness during structured play, as opposed to free-play, when the play partner is non-directive.

134.19 19 Correlation Between Play and Turn-Taking in Young Children with Autism. R. G. Lieberman*[1], P. Yoder[2] and A. Scott[3], (1)*Peabody College, Vanderbilt University*, (2)*Vanderbilt University*, (3)*Hume-Fogg Magnet School*

Background: Early intervention strategies for young children at-risk for autism focus heavily on increasing early social and language skills.

Oftentimes, these strategies incorporate object play and social games as ways to elicit child communication and social engagement. Social games involve children and adults using predictable, repetitive turns around a central theme, such as an object. Playing such games may help young children with autism learn to coordinate attention to objects and people, an important aspect of learning to intentionally communicate. Children with autism vary in their object interest and object knowledge. Clinical experience indicates that it is more difficult to get children with low object interest or object knowledge to engage in turn-taking games.

Objectives:

This study seeks to test this clinical impression by testing whether there is a positive association between object interest and object knowledge within turn-taking exchanges with an adult.

Methods:

A concurrent correlational design was used to address whether there is an association between object play and turn-taking in young children with autism. Participants included 36 children, average age 33 months (SD = 8). Thirty-three children received a diagnosis of autism by a licensed clinical psychologist using the ADOS and MSEL. Three children received a diagnosis of PDD-NOS. Three variables were derived: (a) number of types of differentiated play actions, (b) number of toys with which differentiated play occurred, and (c) the sum of the number of action turns and give turns taken by the child. The object play variables were derived from the Developmental Play Assessment (Lifter, 2001). The turn-taking variable was derived from an experimental measure of object turn-taking (adapted from Ousely, 1997; Yoder & Stone, 2006).

Results:

The predictions were confirmed. A strong positive correlation was found between number of turns and the number of toys on which differentiated play occurred, and the number of types of differentiated play actions, R-square = 0.284 and 0.2725 respectively.

Conclusions:

This correlational study is a first step in understanding the association between object play and turn-taking. The concurrent correlational design does not identify directionality of the association, nor does it allow for inferences of causation. Therefore, directionality of the association between object play and turn-taking, as well as examination of a possible functional relation between the variables, should be done through rigorous experimental design where threats to internal validity are controlled, and where alternative explanations may be more readily ruled out. If future studies replicate the association and support a causal influence of play on turn-taking, then interventions targeting the increase of children's object interest and object knowledge may increase opportunities for social and language development through turn-taking exchanges. These findings are particularly important as researchers work to develop potential interventions for young children with autism that are effective and family-friendly.

134.20 20 Affective Signaling of Children with Autism: Listeners Prefer the Laughs of Children with Autism. W. J. Hudenko* and M. A. Magenheimer, *Ithaca College*

Background: Despite a growing body of research on the emotional expressions of children with autism, comparatively little is known about the impact of these expressions on others. Understanding the impact of emotional expressions is vital because many expressions, such as laughter, are critical for developing and maintaining relationships with peers and caregivers. Objectives: The purpose of this study was to investigate the impact of laugh sounds produced by children with and without autism on naïve listeners. Given that qualitative differences have been observed between the laughs of children with autism and those of typically developing (TD) children, we also hypothesized that listeners would be attentive to subtle differences between the laughs, thus allowing them to correctly judge which child produced the laugh. Methods: Participants consisted of 135 college-aged individuals (M age = 19.2, 66% Female). In the first part of the study, participants listened to 40 laugh sounds (half were produced by a child with autism and half by a TD child matched on chronological age). Laughs were randomly selected from a sample of 765 laughs obtained from a prior investigation. Participants rated their affective response after listening to each laugh. In the second half of the study,

participants were told that laughs were produced by one of the two groups. Listeners heard 76 laughs and were asked to judge which child produced each laugh. Like the first half of the study, children with autism produced 50% of the laughs, and laughs were randomly selected. Before completing the study, participants were asked to describe the criteria they used to make their judgments and how much experience they had with autism. Results: Results showed that listeners rated the laughs of children with autism more positively than the laughs of TD individuals ($p<.001$), and that they were above chance levels at judging whether the laughs were produced by children with autism ($p<.01$). Females preferred the laughs of both children with autism and those of TD children significantly more than males ($p<.05$). Grounded theory analysis revealed that most participants were listening for acoustic qualities of the laughs such as pitch, volume, or length when making judgments. Despite their accurate judgments, only 19% of participants thought that they could tell the difference between the laughs. No measured variables predicted accuracy. Conclusions: Results from our study suggest that listeners prefer the laughs of children with autism to those of TD children. This preference may be due to subtle acoustic differences in the laughs that mark of the presence of genuine positive affect in children with autism. In contrast with some claims suggesting that children with autism exhibit deficits in their emotional abilities, the current data provide evidence that laughter represents one area where these children are relatively unimpaired. More importantly, our results show that children with autism posses an innate tool that may promote the formation of relationships.

134.21 21 The Role of Intersensory Redundancy in the Typical Development of Social Orienting across Infancy: a New Hypothesis for Autism. J. T. Todd, L. E. Bahrick*, I. Castellanos, B. M. Sorondo, M. Vaillant-Molina and M. A. Argumosa, *Florida International University*

Background: Children with autism show impairments in social orienting and attention. Understanding these impairments requires understanding the typical development of social orienting across infancy, the period during which it develops. However, no research has systematically assessed changes in attention to social versus nonsocial events across infancy. According to the Intersensory Redundancy Hypothesis (IRH, Bahrick & Lickliter, 2002), infants show heightened attention to multimodal events that provide intersensory redundancy (synchrony, rhythm, tempo common to audible and visible stimulation). Relative to nonsocial events, social events provide an extraordinary amount of intersensory redundancy (across face, voice, and gesture). We hypothesize that if sensitivity to intersensory redundancy underlies the development of social orienting, then infants should show differences in basic measures of attention across age as a function of redundancy. A slight disturbance of intersensory processing could then promote social orienting impairments in autism.

Objectives: We assessed the typical developmental trajectory of attention to social and nonsocial events that provide intersensory redundancy (audiovisual) versus no redundancy (unimodal visual) across the ages of 2-8 months. We predicted greater attention (more processing time and fewer disengagements) to events with more redundancy: audiovisual social and nonsocial events > unimodal visual social and nonsocial events, and audiovisual social events > than all other event types, given that social events typically amplify redundancy.

Methods: Data from 705 infants at 2, 3, 4-5, or 6-8 months of age (N = 140, 157, 239, and 169, respectively) were analyzed. Infants were habituated to dynamic displays of bimodal audiovisual versus unimodal visual (silent) social events (women speaking in infant-directed speech) or bimodal audiovisual versus unimodal visual nonsocial events (toy hammer tapping a rhythm). Mean looks away per minute (disengagement) and mean length of time to habituation (processing time) were evaluated.

Results: Age (2, 3, 4-5, 6-8 months) x event type (social, nonsocial) x condition (unimodal, bimodal) between subjects ANOVAs indicated main effects of age with decreasing processing time and increasing disengagements across age, *p*s < .001. Consistent with our predictions, main effects of condition and event type indicated longer processing times and less disengagement for social than nonsocial events (*p*s < .005) and for bimodal redundant than unimodal nonredundant stimulation (ps < .001). These main effects were each qualified by interactions with age (*p*s < .01) where differences between conditions were most apparent for older infants. Slope analyses indicated that attention to

bimodal, redundant social events was maintained across age ($p > .10$), whereas attention to all other event types decreased across age ($p < .01$).

Conclusions: Consistent with predictions of the IRH, these findings demonstrate that attention (processing time and disengagement) to bimodal, redundant social events is maintained across age, from 2-8 months, whereas attention to unimodal and nonsocial events declines across this period. These are the first findings indicating that social orienting develops gradually across infancy, emerging by 3 months, and is a function of intersensory redundancy. Together with findings of impaired intermodal functioning in autism, these findings suggest that intermodal processing disturbance may underlie social orienting impairments in autism.

134.22 22 The Impact of the Brain Overgrowth in Autism on Inter-Hemispheric Connectivity. J. D. Lewis*[1], R. J. Theilmann[2], A. J. Lincoln[3] and J. Townsend[2], (1)*Montreal Neurological Institute, McGill University*, (2)*University of California, San Diego*, (3)*Alliant International University*

Background: Ringo *et al* (1991) hypothesized that, due to the larger metabolic costs and conduction delays associated with long-distance fibers, species with larger brains would show decreased long-distance connectivity. That hypothesis is supported by computational modeling (Ringo *et al*, 1991) and cross-species MRI findings (Rilling and Insel, 1999). A negative relation between brain size and connectivity has also been shown in humans (Jancke *et al*, 1997, Lewis *et al*, 2008). This scaling relation has been found in adults in all regions of the callosum except the isthmus, but is only present in children in the two sub-regions of the callosum which have the longest interhemispheric connections (Lewis *et al,* 2007; 2008). The contrast suggests an impact of connection length on axonal remodeling (Lewis *et al*, 2004; 2007; 2008). This motivates the hypothesis that the abnormal early brain overgrowth seen in autism (Courchesne *et al,* 2001; Hazlett *et al,* 2005) will lead to a lesser degree of long-distance connectivity (Lewis *et al*, 2005; 2008) — consistent with findings of underconnectivity in autism (Just *et al*, 2004; 2005; 2007). The frontal lobes are the locus of the early brain overgrowth in autism (Carper et al, 2005), and so degree of long-distance connectivity should be most reduced in anterior regions of the callosum.

Objectives: The goal of this research was to test the prediction that individuals with autism will show a negative relation between callosal fiber length and degree of interhemispheric connectivity, as do controls, but with a lesser degree of interhemispheric connectivity between the frontal lobes.

Methods: Using diffusion tensor imaging (DTI) and tractography to detail the patterns of connectivity of the corpus callosum, and to estimate the length of interhemispheric fibers in each of five sub-regions, we investigated the relation between callosal fiber-tract length and degree of interhemispheric connectivity in 20 young adult males with autism and 22 controls. Regression analyses were used to assess the scaling relation in each of the five sub-regions in both groups, and between group differences were assessed with analysis of variance tests.

Results: Regressions of callosal fiber-tract length on degree of interhemispheric connectivity were significant in anterior, mid, and posterior sub-regions in both individuals with autism and in controls. Anterior regions showed a significantly reduced degree of connectivity in the autistic group.

Conclusions: The results support the hypothesis that the early brain overgrowth in autism leads to reduced connectivity.

134.23 23 Functional Connectivity Abnormalities during Self-Referential Cognitive Processing in Autism Spectrum Conditions. M. V. Lombardo*[1], B. Chakrabarti[1], E. Bullmore[2], S. A. Sadek[1], G. Pasco[3], S. J. Wheelwright[4], J. Suckling[5], S. Baron-Cohen[4] and M. R. C. AIMS Consortium[6], (1)*University of Cambridge, Autism Research Centre*, (2)*Brain Mapping Unit, University of Cambridge*, (3)*Autism Research Centre, Department of Psychiatry, University of Cambridge*, (4)*University of Cambridge*, (5)*Brain Mapping Unit, Department of Psychiatry, University of Cambridge*, (6)*University of Cambridge; Institute of Psychiatry, King's College London; University of Oxford*

Background: Individuals with autism spectrum conditions (ASC) have broad impairments in self-referential cognition (Lombardo et al., 2007, PLoS One). The underlying neural mechanism for these impairments appears to be localized in the ventral medial prefrontal cortex (vMPFC). We explored the distributed neural circuit in which vMPFC participates (via functional connectivity methods) during self-referential judgments.

Objectives: To assess functional connectivity patterns from vMPFC during self-referential judgments, in people with and without ASC.

Methods: 30 adult males (18-45 years old) with a diagnosis of Asperger Syndrome and 33 age-, sex-, and IQ-matched neurotypical adults were scanned at 3T during fMRI while making mentalizing or physical judgments about themselves or a non-close other. Functional connectivity analyses were implemented with psychophysiological interaction (PPI) analyses in SPM5.

Results: Neurotypical adults exhibited a clear pattern of functional connectivity from vMPFC during Self>Other judgments. This pattern of increased functional connectivity during self-referential judgments extended into anterior insula (AI), ventral premotor cortex (PMv), somatosensory cortex (SI/SII), and middle cingulate cortex (MCC). This functional connectivity pattern was absent among the ASC group. Group differences between Controls>ASC illuminated this absence of significant functional connectivity in the ASC group. When exploring the Self-Mentalizing>Self-Physical contrast, the ASC group showed more vMPFC functional connectivity than neurotypicals within areas associated with the default mode network, such as posterior cingulate/precuneus (PCC) and temporo-parietal junction (TPJ).

Conclusions: These results demonstrate that the underlying computations occurring during self-referential cognitive processes in ASC are severely limited in their implementation throughout the brain. Individuals with ASC do not show the normative pattern of vMPFC engagement during self-referential judgments. Futhermore, the normative functional connectivity pattern that arises from recruitment of vMPFC is absent in the ASC group. Thus, not only is processing atypical in vMPFC, but distributed neural processing across an entire neural circuit important for self-referential cognitive processes also appears to be abnormally organized. These results are also important because they highlight that normative vMPFC functioning during self-referential cognitive processing relies on the interactions between other areas associated with embodied representations such as anterior insula, somatosensory cortex, ventral premotor cortex, and middle cingulate cortex. What is most striking is that individuals with ASC do not recruit these regions in tandem with processing in vMPFC. Such an observation goes further into describing the neural mechanisms underlying the atypical organization of self-referential cognitive processes in ASC. Finally, the observation of increased vMPFC functional connectivity with the default mode network during Self-Mentalizing judgments may signal that the deficit in self-mentalizing arises from the vMPFC being unable to disengage its interactions with the default mode of functional brain organization and shift into task-specific processing for the mentalizing task at hand.

134.24 24 Transverse Relaxation Time Imaging of Frontal Lobe White Matter in Autism. R. Spring*[1], N. Rajakumar[1], Y. Gagnon[1], D. Drost[1] and R. Nicolson[2], (1)*University of Western Ontario*, (2)*The University of Western Ontario*

Background: Transverse relaxation time (T2) is a quantitative Magnetic Resonance Imaging (MRI) technique that has the potential to increase our understanding of the aberrant brain development underlying autism. T2 is influenced by tissue water content, with longer T2 reflecting increased "free" water content. Previous studies by our group have found increases in total white matter T2 in patients with autism using automated region of interest (ROI) segmentation.

Objectives: The purpose of this study was to examine frontal lobe white matter T2 relaxation to determine if total white matter increases were localized to the frontal lobes which have been previously implicated in autism.

Methods: Nineteen males with autism (age: 9.2 ± 3.0 years) and 20 male controls (age: 10.7 ± 2.9 years) underwent a magnetic resonance imaging study at 3.0 Tesla. T2 and proton-density weighted images were acquired and quantitative T2 maps were generated from the GESFIDE MRI acquisition (Ma and Werhli, J. Magn. Reson. 111:61-69, 1996). Right, left and total frontal lobe white matter were hand traced in Analyze and mean T2 was calculated in the selected regions.

Results: The groups did not differ significantly in demographic variables, although patients with autism did have a significantly lower verbal IQ. Preliminary results on a subset of 14 patients and 14 controls revealed that patients with autism had a significant increase in total frontal white matter T2 (p<0.04). There were no significant group

differences in left or right frontal white matter T2.

Conclusions: The present results need to be considered as preliminary, particularly given the small sample size and the inclusion of males only. The increases in frontal white matter T2 in patients with autism likely reflects increased tissue water, which is consistent with other studies indicating an increase in the volume of frontal white matter in autism. The increased tissue water could be secondary to fluid within myelin or inflammation, either of which could cause abnormalities of neurotransmission within the frontal lobes and reduced cortical connectivity.

134.25 25 Brain Function and Connectivity during Attention Orienting in Autism Spectrum Disorder. J. McGrath*[1], K. Johnson[2], H. Garavan[2], M. Gill[1], C. Ecker[3] and L. Gallagher[1], (1)*Trinity College Dublin*, (2)*Trinity College Institute of Neuroscience*, (3)*King's College London, Institute of Psychiatry*

Background: Spatial orienting of attention is a cognitive function that allows a person to move their attentional focus from one location to another location in response to a stimulus. Attention orienting can be triggered in two ways; exogenously and endogenously. Exogenous attention orienting refers to the shift in attentional focus that occurs in an automatic, reflexive manner in response to sudden onset stimuli. Endogenous attention orienting describes voluntary, goal-driven shifting of attention; for example in response to a cue that signals where to look or listen.
Orienting attention to new and important sources of information is crucial for learning and normal socio-emotional development. The majority of the attention cuing literature suggests that exogenous, stimulus-driven attention orienting is impaired in Autism Spectrum Disorder (ASD). Surprisingly, only a handful of studies have examined endogenous orienting in ASD and the findings are inconsistent. Difficulties in attention orienting may contribute to the development of a number of core features of ASD. It has been suggested that abnormal joint attention, unusual eye contact, lack of response to auditory or visual stimuli and slowed shifting of attention could all result from an underlying deficit in attention orienting. Dysfunctional attention orienting may be an important factor contributing to social communication difficulties in autism.
Attention orienting appears to be subserved by two interacting networks. A bilateral dorsal frontoparietal network is involved in endogenous goal-directed attention orienting, whereas a largely right lateralised ventral frontoparietal system is activated during stimulus-driven attentional orienting. It is thought that this ventral network functions as a circuit breaker for the dorsal network and directs attention to behaviourally relevant stimuli outside the focus of processing.
Recent neuroimaging research has revealed abnormal interregional functional connectivity in ASD during a variety of cognitive tasks. This study aims to investigate whether there is abnormal functional connectivity between frontal and parietal regions in the ASD group during this task.
Objectives: To compare brain activation and functional connectivity during exogenous and endogenous attention orienting in individuals with ASD and controls.

Methods: Participants with ASD and age and IQ matched controls will perform a Posner style attention orienting task during functional MRI in a 3T scanner. Presentation of a central arrow cue activates endogenous goal-directed attention orienting. When the target is invalidly cued, i.e. appears at an unexpected location, exogenous, stimulus driven attention orienting is activated. Regions of brain activation are compared between cases and controls using AFNI software. Functional connectivity analysis will be performed.

Results: Preliminary results are in keeping with the research that suggests that two frontoparietal networks are involved in goal directed and stimulus-driven attention orienting. Recruitment and testing is ongoing.
Conclusions: Based on prior evidence from the literature, we expect to see significant brain activation differences between cases and controls during fMRI. Based on a number of recent studies of functional connectivity in ASD, we expect to find abnormal interregional connectivity in the ASD group. These findings will be important for our understanding of brain function in ASD.

134.26 26 White Matter Connectivity and Autism Clinical Symptomatology: a Diffusion MRI Study. A. Bargiacchi*[1], A. Cachia[1], N. Chabane[2], N. Boddaert[3], A. Philippe[4], F. Brunelle[4], M. C. Mouren[2], Y. Samson[5], L. Laurier[1] and M. Zilbovicius[1], (1)*Research Unit U797 "Neuroimaging and Psychiatry", CEA - INSERM*, (2)*Hospital Robert Debre*, (3)*Hospital Necker*, (4)*Necker Hospital*, (5)*Pitié-Salpêtrière Hospital*

Background:

Anatomo-functional abnormalities in the regions of the 'social brain' (superior temporal sulcus, orbito-frontal cortex, amygdala and fusiform gyrus) have previously been described in autism spectrum disorders (ASD) . Besides, several studies have reported reduced fronto-temporal functional connectivity among this network . More recently, diffusion neuroimaging techniques have also pointed out ASD-associated white matter abnormalities, suggesting anatomical connectivity disruptions in this disorder .

Objectives:

In our study we tested the hypothesis of a relationship between white matter integrity and two clinical characteristics of children with ASD: autism severity and verbal communication deficit.

Methods:

White matter integrity was voxel-wise assessed over the whole brain using high-angular resolution diffusion tensor imaging (DTI) in 24 children with ASD (age = 8.4 ± 3.5 years; IQ = 65.2 ± 24.6; mean ± SD). The ASD diagnosis was based on DSM IV-R and ADI-R criteria. Autism clinical severity was assessed with ADI-R total score. High angular resolution diffusion images (HARDI) were acquired on a GE-Signa 1.5 T using an echoplanar sequence (41 directions, TE=70 ms; TR=9000 ms; 2*1.8*1.8 mm3; b=1500 s/mm2). Fractional anisotropy (FA) & apparent diffusion coefficient (ADC) maps were estimated with Brainvisa software (http://brainvisa.info) and then non linearly spatially normalized on study-specific FA template and spatially smoothed (8 mm) using SPM5 software (http://www.fil.ion.ucl.ac.uk/spm/).

Two statistical analyzes of FA and ADC maps were performed: 1) correlation analysis with autism severity (total ADI-R score) and 2) comparison between ASD children with language vs. ASD children without language. Analyses, controlled for age and IQ, were performed on the whole brain using a voxelwise threshold at $p < 0.005$.

Results:

We found a significant correlation between ASD severity and white matter microstructure in the main pathways of the social brain network (arcuate and uncinate fasciculi): the more severe the autistic syndrome, the more FA reduction and the more ADC increase in these regions. We also found white matter microstructure differences between ASD children with and without language in white matter regions of the language network: temporal pole, superior and middle temporal regions, inferior frontal region (temporal and frontal parts of the arcuate fasciculus). In these regions, the FA was higher and the ADC was lower in the ASD children with verbal communication.

Conclusions:

In this first high resolution whole-brain analysis of diffusion indices in children with ASD, we found a correlation between autism severity and white matter disruption in fronto-temporal pathways. We also found white matter differences in the arcuate fasciculus according to the presence or absence of language. Our results suggest white matter disorganization and/or reduced myelination in ASD, and support abnormal anatomical connectivity in ASD within the social and the language networks.

134.27 27 Reduced Intrinsic Connectivity in the Default Network in Adolescents with Autism Spectrum Disorders. S. J. Weng*, S. Peltier, J. L. Wiggins, M. Carrasco, C. Lord and C. S. Monk, *University of Michigan*

Background: ASD is associated with disturbances of neural connectivity. Connectivity is typically examined within the context of a cognitive task. However, connectivity also exists in the absence of a task. This intrinsic connectivity, known as resting-state connectivity is particularly active in a set of structures called the default network, which includes the posterior cingulate cortex (PCC), retro-splenial cortex, lateral parietal cortex/angular gyrus, medial prefrontal cortex, superior frontal gyrus, temporal lobe, and parahippocampal gyrus. Exploring resting-state connectivity in ASD is of interest as these networks might be active during self-referencing and introspection, domains in which deficits in empathy and social cognition hinge upon. In addition, no prior study has explored resting-state connectivity within adolescents with ASD.

Objectives: We sought to examine resting-state connectivity within the default network in adolescents with ASD and to examine how various measures of symptom severity and adaptive functioning relate to patterns of connectivity.

Following the results from a previous resting connectivity study in our lab that showed patterns of weaker and tighter connectivity in adults with ASD, we hypothesized that adolescents with ASD would show weaker coupling between the PCC and the superior frontal gyrus relative to controls. Second, we hypothesized that adolescents with ASD would show tighter coupling between the PCC and the superior temporal gyrus and parahippocampal gyrus relative to controls. Finally, in an exploratory analysis we sought to examine if symptom severity was associated strength of connectivity.
Methods: 12 adolescents with ASD and 12 age-matched controls between the ages of 13-17 took part in a functional MRI study. Participants were instructed to "let your mind wander freely" while looking at a fixation cross displayed in the middle of the screen for 10 minutes during fMRI acquisition. A seed region was placed in the PCC and functional connectivity was examined by obtaining the correlational activity between the PCC and other areas of the default network.
Results: Both ASD and control groups activated the default network of the brain at $p<0.05$ (whole brain corrected). Analyses of group differences revealed that individuals with ASD relative to controls showed weaker connectivity between the PCC and all regions in the default network ($p<0.05$ small volume corrected). Moreover, ASD relative to the control groups showed tighter connectivity between the PCC and the superior temporal gyrus. A correlation analysis revealed that poorer social functioning was associated with weaker connectivity between the PCC and left angular gyrus. Greater impairments in the restricted and repetitive behavior domain were associated with weaker connectivity between the PCC and the temporal lobe. Finally, lower overall adaptive functioning in the ASD group was associated with weaker connectivity between the PCC and the angular gyrus.
Conclusions: Relative to the control group, the ASD group showed weaker functional connectivity within the default network in the absence of a task. In addition, more severe symptoms were associated with weaker connectivity within the default network. These findings suggest evidence for altered connectivity within the default network and that connectivity between these structures is associated with core impairments in ASD.

134.28 28 Neural Basis of Action and Intention Understanding in Autism and Typical Development. N. Hatt*[1], C. Colombi[2], C. D. Saron[3], S. J. Rogers[4] and S. M. Rivera[3], (1)*University of California, Davis*, (2)*UMACC*, (3)*University of California at Davis*, (4)*M.I.N.D. Institute, University of California at Davis*

Background:
The mirror neuron system (MNS) is comprised of interconnected brain regions whose neurons respond in a similar way whether an individual is observing or executing an action. Some define the MNS strictly as an action observation-execution matching system, while others assert that it supports intention understanding and empathy. It follows that such a system would be impaired in autism, and several studies have found preliminary evidence for this hypothesis (e.g. Oberman et al., 2005). Recent experimental work suggests that children with autism are not impaired in all the functions thought to be supported by the MNS (Carpenter et al., 2001), making it hard to reconcile the hypothesis of a global MNS impairment in ASD with the ability to understand intentional acts on objects.This study is a counterpart to a recent EEG study from our group that exploring the hypothesis with mu wave suppression as the indicator of MNS activity. In the current fMRI study, we examine the same experimental participant group, using the same experimental stimuli for one paradigm while expanding it with a second, complementary, paradigm.

Objectives:
The objective of this research is to reconcile the aforementioned inconsistency by comparing indices of MNS activation in children with ASD to those with typical development (TD). The study explores MNS activation in response to observation of actions varied by transitivity, visibility and the conventionality of underlying intention. We hypothesize that, compared the matched TD control group, children with ASD will demonstrate abnormal patterns of response during observation of other people's intransitive actions and actions for unconventional intentions.

Methods:
Neuroimaging and psychological measures were obtained from the two participant groups. During functional neuroimaging, participants viewed videos of transitive and intransitive grasping actions, with the hand-to-object grasp occluded by a screen for half of the stimuli, and videos of actions demonstrating conventional and unconventional intentions. The behavioral

measures assessed general cognitive skill, imitative ability and intention understanding.

Results:
Preliminary neuroimaging analyses show that TD participants and participants with ASD display neural activation in the inferior frontal gyrus and inferior parietal lobe, key components of the MNS, while viewing actions on objects and actions that indicate conventional intentions. Both groups show negligible MNS activation when viewing intransitive actions. These early findings also replicate Umilta's study, showing a main effect for transitivity (Umilta et al., 2001) with negligible effect of the visibility of the final grasping (or mimed grasping) action. Consistent with the behavioral imitation literature, the MNS of participants with ASD was more robust for transitive compared to intransitive actions. Similarly, we are finding different MNS activation patterns for actions demonstrating conventional contrasted with unconventional intentions. The MNS activation of TD participants is showing a main effect of intention conventionality, while that of the ASD is not.

Conclusions:
These preliminary analyses support our hypothesis that there is not a gross absence of MNS activation in children with ASD. Indeed, there seems to be typical MNS activation for paradigms depicting behaviors with which children with ASD have preserved competency, namely imitating transitive actions.

134.29 29 The Potential Contribution of the Left IFG to the Autistic Phenotype: a Case Study of Monozygotic Twins. K. A. Kellett*, J. L. Stevenson, B. A. Vlach, H. H. Goldsmith and M. A. Gernsbacher, *University of Wisconsin-Madison*

Background: The left inferior frontal gyrus (IFG) plays a fundamental role in communication. The left IFG is considered a classic speech center, to which focal lesions ablate speech (e.g., Alexander et al., 1990), and transcranial magnetic stimulation not only arrests overt speech (Thiel et al., 2005) but also covert speech (Aziz-Zadeh et al., 2005). Moreover, transcranial magnetic stimulation to the left IFG, in particular BA 44, disrupts volitional hand movement, such as that used in nonverbal communication and gesture (Uozumi et al., 2004).
Objectives: To examine the contribution of the left IFG to the autistic phenotype by examining a pair of monozygotic twins.
Methods: Participants were a pair of monozygotic twins recruited into a statewide sample of twin pairs in which one or both cotwins had received a community diagnosis on the autism spectrum. Both cotwins were screened with the SRS and SCQ at age 13;6, were assessed with the ADOS at 15;6, and underwent structural MRI at 17;8. Both twins, born from an unremarkable pregnancy, had received an unorthodox community diagnosis of "Asperger Syndrome with speech delay" at age three. When assessed during adolescence, the twins were comparable on two measures of nonverbal intelligence (Leiter International Performance Scale and Ravens Standard Progressive Matrices) and on two measures of receptive language (Test of Receptive Grammar and Peabody Picture Vocabulary Test). A re-test, two years later, on the Peabody Picture Vocabulary Test continued to show strong similarity between the two cotwins (Twin A PPVT standard score=108; Twin B PPVT standard score=111).
The twins differed dramatically on the Expressive Language Scale of the CELF-3. Twin A scored consistently lower on each of the three expressive subtests -- Recalling Sentences, Sentence Assembly, and Formulating Sentences – and received a significantly lower standard score (Twin A Expressive Language standard score=75, 90% CI=67-83; Twin B Expressive Language standard score=96, 90% CI=88-104).
Twin A exceeded by 1 point the SCQ "autism" cutoff, and Twin B exceeded by 1 point the SCQ "autism spectrum" cutoff. Twin A exceeded by 1 and 2 points, respectively, the "autism" cutoff on the ADOS Communication and Social Interaction scales, whereas Twin B exceeded by 1 point the "autism spectrum" cutoff for Social Interaction but missed by 1 point the "autism spectrum" cutoff for Communication. Finally, Twin A exceeded by 2 points the SRS cutoff for "severe" diagnoses, whereas Twin B missed by 6 points the SRS cutoff for "mild to moderate" diagnoses.
Results: Using a 3T GE-Signa MRI scanner, 3D T1-weighted, inversion-recovery prepped, fast-gradient echo images were acquired for each twin (TR=8.4 ms, TE=1.7 ms, TI=600ms, FOV=240x240mm, flip angle=10 degrees, 256x192 matrix, 124 axial slices, slice thickness=1.2mm). The right IFG for each twin was similar in sulcal contour. In contrast, the anterior ascending ramus and anterior horizontal ramus of the left IFG of Twin A formed more of a Y-shape, whereas Twin B's formed more of a J-

shape.
Conclusions: This case study of monozygotic twins raises the possibility that epigenetic factors may influence the structure of the left IFG.

134.30 30 Chemical Shift Imaging and Single Voxel Magnetic Resonance Spectroscopy in High Functioning School-Aged Boys with ASD and Typical Development. E. Ratai[1], N. Shetty*[1], M. Herbert[1] and A. P. Ringer[2], (1)*Massachusetts General Hospital*, (2)*University of California, Berkeley*

Background: The tissue nature of brain enlargement in young autistic subjects has not yet been clearly established. Published findings do not support an increase in neuronal density in gray matter or the attribution of white matter enlargement to an increase in myelinated fibers. Given the growing documentation of metabolic findings in autism, these brain changes need to be investigated using techniques sensitive to metabolites. Frontal and prefrontal white matter enlargement is particularly prominent and its metabolic underpinnings need to be targeted using magnetic resonance spectroscopy (MRS) methods. Objectives: To investigate metabolic alterations in ASD brain tissue collected using single voxel spectroscopy and chemical shift imaging.
Methods: Proton magnetic resonance spectroscopy was performed with a 3T Siemens scanner on age matched typically developing and children with Autism Spectrum Disorders (6-13 year olds). Single Voxel Spectroscopy (SVS) was acquired with the voxel placed on the left prefrontal white matter; Chemical Shift Imaging (CSI) was acquired with the grid placed centrally covering prefrontal white matter as well as over portions of corpus callosum, parietal gray matter, prefrontal grey matter, caudate, thalamus, and parietal gray matter regions. The spectra were processed offline using LCModel, a user independent fitting routine.
Results: We will present our findings where significant differences were observed ($p<0.05$) and where no significant differences were observed ($p>0.05$) in ratios and absolute concentrations of N-Acetylaspartate, choline, *myo*-Inositol , glutamine/glutamate , creatine and lactate in the investigated regions.
Conclusions: The identification of metabolic alterations by MRI in ASD helps characterize the tissue dimension of brain alterations in this complex condition and to sharpen hypotheses regarding linkages between tissue pathophysiology and cognitive neuroscience.

134.31 31 Hemispheric Lateralisation of Neural Responses to Faces in Individuals with Autism: a Magnetoencephalographic Study. S. Braeutigam*[1], A. Kylliainen[2] and A. Bailey[1], (1)*University of Oxford*, (2)*University of Tampere*

Background: It is commonly agreed that laterality is a fundamental feature associated with brain functioning under normal conditions. Recent findings obtained from electrophysiological and neuroimaging studies provide evidence for lateralised anomalies in the neural response in individuals with autism spectrum disorders compared to typically developing individuals. However, it is unresolved whether such anomalies reflect qualitative changes in laterality rather than quantitative modulation of neural activity without affecting hemispheric patterns in general.

Objectives: To investigate hemispheric differences in the neural response associated with face processing using magnetoencephalography.

Methods: 8 male individuals with autism and 8 typically developing male subjects participated in this study. Participants were matched on age (mean 12 years) and IQ. All measurements were taken at the Brain Research Unit, Helsinki University of Technology, using a VectorView(TM) system providing first-order gradiometers most sensitive to directly underlying neuronal currents. The participants performed a matching task that required attention to be paid to the identity of images, where pairs of images of adolescents with varying gaze direction and motorbikes were presented sequentially. This study was approved by the ethics committee of Tampere University, and all participants and their parents gave informed consent before experimentation.

Results: At 100 ms after stimulus onset, all image categories evoked stronger responses over right compared to left extra-striate cortices in both groups, however the responses detected over the right hemisphere were significantly stronger in individuals with autism compared to typically developing subjects. In typically developing individuals, straight gaze evoked significantly stronger activity over left anterior cortices at around 340 ms compared to averted gaze. The opposite pattern, averted stronger than straight, was found in individuals with autism over approximately the same region and latency. These findings will be compared to results obtained from an analysis of asymmetry of alpha-band power.

Conclusions: These data suggest that laterality changes in autism are bound to be multifaceted, being both quantitative and qualitative dependent

on stimulus type and processing stage. This may have implications for inferring the functional neuroanatomy in autism based on known correlation of brain activity and task parameter established in typically developing individuals.

134.32 32 EEG Study of Mirror Neuron Functioning in Infants with Autism Spectrum Disorder. H. Roeyers*[1], L. Ruysschaert[1], P. Warreyn[1], G. Pattyn[1], A. Handl[2] and J. R. Wiersema[1], (1)*Ghent University*, (2)*Max Planck Institute for Human Cognitive and Brain Sciences*

Background: It is quite well known that imitation is impaired in young children with autism spectrum disorder. In primates as well as in humans, imitation has been linked to a group of visuomotor neurons called 'mirror neurons', which also fire during action observation. This led to the hypothesis of a dysfunctional mirror neuron system (MNS) in individuals with ASD (Williams et al., 2001). Some support for this hypothesis was found in adults and children, although not all studies found evidence of an impaired MNS in ASD. Research into the MNS with infants remains scarce.

Objectives: Suppression in the EEG mu rhythm band is associated with the MNS activity and was previously investigated in adults and children with and without ASD. In this study, we apply a child-friendly paradigm to investigate mu wave suppression during action observation and action imitation in typically developing infants and infants with a diagnosis or marked characteristics of ASD (age 18-30 months). Following Marchall and colleagues (2002) and Stroganova and colleagues (1999), we defined infant mu wave within the 6-9 Hz frequency range.

Methods: The experiment consisted of 5 blocks (with 5 different objects) and one free play situation (including all 5 objects) during which brain activity was measured on 32 active electrodes. In each block, the infants observed a moving object (object observation condition) and an experimenter performing hand movements (hand movement condition). Subsequently, infants watched (action observation condition) and imitated (action imitation condition) a simple goal-directed action with each object. At the end of the experiment infants were imitated by the experimenter while playing with the objects (free play condition). Hand movement condition and action observation/imitation were counterbalanced between subjects.

Results: 40 infants participated in the study. Preliminary analyses revealed that typically developing infants and infants with (characteristics of) ASD showed significant mu wave suppression on frontal, central, and parietal electrodes during action imitation and play conditions. This suggests that the locations and frequency band were appropriately defined for detecting sensorimotor brain activity. Typically developing infants also displayed mu suppression during the hand movement, and to a lesser extent during the action observation condition. The infants with (characteristics of) ASD showed little mu suppression during the hand movement condition, and none during action observation.

Conclusions: These preliminary results support the presence of a mirror neuron system in typically developing infants, especially during the observation of hand movements. Mirror neuron activity seems to be less pronounced in infants with (characteristics of) ASD.
Full results and conclusions will be presented at the IMFAR meeting.

134.33 33 Event-Related Potential Study of the Effects of Repetitive Transcranial Magnetic Stimulation on Novelty Processing in Autism. M. F. Casanova*, E. M. Sokhadze, L. Sears and J. M. Baruth, *University of Louisville*

Background: Autism is considered to be a neurodevelopmental disorder characterized by severe disturbances in social relations, impaired development of language and communication skills, and a limited repertoire of behavioral patterns. Neuropathological findings by our group have indicated an increased number of cortical minicolumns with less surrounding neuropil space in the dorsolateral prefrontal cortex (DLPFC) of individuals with autism. Less minicolumnar neuropil space in the DLPC is indicative of a lack of GABAergic inhibitory interneurons leading to an alteration of the excitation-inhibition balance in the DLPFC and lower signal-to-noise ratio. The DLPFC is functionally interconnected with other cortical areas involved in cognitive functions. Repetitive transcranial magnetic stimulation (rTMS) administered at frequencies ≤1 Hz over the DLPFC has proven to increase the amount of inhibitory activity of the stimulated cortical region in studies on depression and anxiety disorders.

Objectives: This study investigated potential positive effects of low frequency rTMS on processing of novel distracters in a visual three-

stimulus oddball task in children and young adults with autism.

Methods: To test the effects of rTMS in autism we recruited 11 individuals with a primary diagnosis of an autism spectrum disorder (ASD) and 11 age-matched controls to participate in an event-related potential (ERP) study of novelty processing before and after six sessions of rTMS. Only autistic individuals were enrolled in the rTMS trial, while controls were tested on the same cognitive test twice within a month. RTMS stimulation consisted of 2 sessions per week for three weeks for a total of 150 pulses (0.5 Hz) per day at 90 % of motor threshold.

Results: In a baseline test we found significantly delayed latencies to novel stimuli in the early (P100, N100), and late (P2a, N200, P3a) ERPs over the frontal lobe in autism relative to controls. We found increased amplitudes of the early frontal ERPs to non-target and novel stimuli in autism as well. These results indicate low selectivity and ineffective filtration in early processing stages and reduced activation of integrative regions in the frontal cortices in autism. Over centroparietal channels we found a significant reduction in the amplitude of the N2b and an increase in the latency of the early N100 component to targets in autism. Also, the P3b showed a significantly delayed latency to novel stimuli. These baseline test results suggest that autistic subjects over-process information needed for successful differentiation of target and novel stimuli in the oddball test. After completion of the rTMS treatment individuals with autism group showed a significant reduction in latency of the late frontal components both to target and novel stimuli. Individuals with autism showed a reduction in latency of the late parietal ERPs to novel stimuli while showing an increase in latency to target stimuli. There were no significant changes of ERP components in the repeated test in control group.

Conclusions: These ERP results suggest improved selectivity in early processing stages over the frontal cortices and more efficient differentiation of target and novel stimuli as a result of rTMS treatment in individuals with autism.

134.34 34 Music and Emotion in Autism: a fMRI Study. S. De Falco, A. Caria, P. Venuti* and G. Esposito, *University of Trento*

Background: Autism Spectrum Disorders (ASD) dramatically impair interpersonal behaviours, sociality and communication. A specific deficit in the ability to express and understand emotions has often been hypothesized to be an important correlate underlying such social impairments. Studies have so far thoroughly explored the deficit of individuals with ASD in identifying emotions in visual stimuli (facial expressions) but little is known about their ability to perceive emotions conveyed by auditory stimuli such as music. Music has been found to be capable to evoke and convey strong and consistent positive and negative emotions in healthy subjects (Koelsch et al 2005, 2006; Mitterschiffthaler et al 2007). Neuroimaging studies on healthy adults have brought to light the neural correlates of emotional processing of music. In particular a network of limbic and paralimbic structures implicated in reward and emotion is observed in response to music (Zatorre 1994; Blood et al 1999; Blood and Zatorre 2001). Research in autism has highlighted a relatively intact or superior musical pitch processing (Bonnel et al 2003; Heaton 2003, 2005; Mottron et al 2000). Yet, behavioural studies on ASD subjects have reported their ability to properly identify the positive or negative emotional valence of music stimuli (Heaton et al 1999, 2001).

Objectives: This study uses functional magnetic resonance imaging (fMRI) to identify the neural correlates of emotion processing in subjects with Autism Spectrum Disorders (ASD) during music perception. The aim is to provide a neurobiological support to the behavioural studies reporting a preserved ability to identify emotions conveyed by music in subjects with ASD.

Methods: Five high-functioning ASD adults subjects (19 and 32 years) participated to the study. The ASD subjects underwent a single fMRI session in a 4T scanner using a passive music listening paradigm with preferred musical excerpts, classical musical excerpts and sequences of random tones. All the stimuli were presented in a blocked design of 30s of musical pieces, 30 s random tones interspersed with a 15s rest period. fMRI data analysis was performed using the SPM5 software (Wellcome Department of Imaging Neuroscience, London). Results: A single subject analysis first contrasted both preferred musical excerpts and classical musical excerpts with a rest period. This analysis revealed activation in auditory temporal pole, with a bias towards the right hemisphere, which is in line with the reported preserved ability of music

processing. A further analysis comparing the musical excerpts excerpts with the sequences of random tones showed a quite heterogeneous pattern of brain activity. In most of the cases preferred but not standard classical excerpts elicited increased activation of limbic and/or paralimbic structures usually involved in emotional processing.

Conclusions: These preliminary results indicate the altered and preserved cerebral brain circuitries involved in the emotional processing of music in ASD subjects . A larger group study may enhance our knowledge of emotional skills and deficit in ASD and may provide the neurobiological bases for the interventions based on music therapy which seem to facilitate communication in ASD subjects (Edgerton et al 1994; Ma et al 2001; Kern et al 2006, 2007; de Falco et al 2006).

134.35 35 Neural Specialization for Faces and Letters in Autism. J. McPartland*[1], J. Wu[1], R. T. Schultz[2] and A. Klin[3], (1)*Yale Child Study Center*, (2)*Children's Hospital of Philadelphia and the University of Pennsylvania*, (3)*Yale University School of Medicine*

Background: Individuals with autism have been shown to exhibit behavioral and neural anomalies in face perception. These have been hypothesized to reflect a lack of expertise resulting from reduced social motivation and consequent inattention to faces during development. Previously presented data collected from a small sample of children with autism reflected preserved neural specialization for non-social information, i.e. letters of the alphabet. The current study investigates perceptual expertise for social and non-social information in a large sample of children with autism and typical counterparts.
Objectives: To compare electrophysiological indices of perceptual expertise for social and non-social visual information in individuals with autism.
Methods: Event-related potentials (ERPs; 256 channel Geodesic Sensor Net) were recorded from high-functioning children with autism and typically-developing peers. Participants viewed social and non-social "expert" versus "non-expert" stimuli (human faces vs. houses, Roman letters versus pseudoletters). Peak amplitude and latency were extracted for a negative component at 170 milliseconds over lateral posterior scalp (N170). Behavioral assessments measured proficiency at letter and face recognition.
Results: Typical individuals displayed expertise effects for the N170 in response to both faces and letters. In contrast, those with autism displayed expertise effects for letters only. ERP parameters and behavioral measures of letter and face perception revealed correlations among processing speed and proficiency. Analyses in progress will localize neural sources of activity using individual-specific 3D head models created with the Geodesic Photogrammetry System.

Conclusions: Results add to the body of literature indicating social brain dysfunction in autism. Despite atypical brain response to faces, children with autism demonstrate intact neural specialization for non-social visual information, letters of the alphabet. Findings suggest preserved capacity for neural specialization when individuals with autism obtain sufficient exposure to and engagement with a visual stimulus class.

134.36 36 When the Archeologist's Career Ended in Ruins: An fMRI Study of Pun Comprehension in Autism. H. M. Wadsworth*[1], L. G. Klinger[2], M. R. Klinger[2] and R. K. Kana[1], (1)*University of Alabama at Birmingham*, (2)*University of Alabama*

Background: Understanding intended and contextual meanings in language is among the most affected aspects of language comprehension in autism (Happe, 1994; Tager-Flusberg, 1981). This difficulty may lie in the fact that comprehension of figurative language, such as irony and pun, may be atypical in autism (Happe, 1995). While several studies have examined other types of figurative language in individuals with autism, no brain imaging study to date has examined pun comprehension in autism. A pun is a rhetorical technique in which the speaker deliberately invokes multiple meanings through a single word or phrase. Comprehending puns is a challenging cognitive task since it involves several subtasks, such as identifying multiple meanings of the word, decoding the pun sentence, and understanding the joke. People with autism might have difficulty in all these processes, and the current study examined the cortical bases of such processes.

Objectives: The primary aim of this study was to investigate the neural mechanisms involved in interpreting figurative language, specifically comprehending puns in autism.

Methods: Seven high-functioning adolescents and adults with autism and nine age and IQ matched controls participated in this fMRI study (data collection in progress). Sentences containing

puns (*e.g. To write with a broken pencil is pointless*) and control sentences were presented visually in a blocked design format with four blocks in each experimental condition. The participants' task was to silently read and understand one meaning (in the literal condition) or two meanings (in the pun condition) in each sentence and press a button to indicate that they had read and understood the sentence. After the scanning session, the participants were asked to point out the two meanings in each sentence.

Results: Participants with autism showed reliably lower levels of activation than controls in left inferior frontal gyrus (pars opercularis aspect) and left middle temporal gyrus while comprehending pun, suggesting difficulty with determining word meaning and deciphering syntactic cues from the pun sentence. In contrast, participants with autism activated more right fusiform gyrus (part of the visual word form area) and right middle temporal gyrus (RMTG), indicating the utilization of a different approach to understanding word meaning. There was also lower activation in the right orbitofrontal cortex (OFC), an area thought to be involved in humor comprehension.

Conclusions: Underactivation in autism in left hemisphere language regions (especially pars opercularis of the IFG) while comprehending puns suggests that participants with autism may not be deciphering the syntactic cues of the sentence or understanding the multiple meanings involved. Greater RMTG activation in autism may corroborate this view by suggesting increased difficulty in comprehending the meanings of the sentence. Moreover, greater activation in autism in the visual word form area while reading pun sentences may suggest their possible focus on graphemic level instead of lexical semantic level. Finally, if participants with autism do not understand the multiple meanings of pun, they may not be detecting the humor (indicated by less activation in OFC). Overall, these findings suggest atypical cortical recruitment in autism while comprehending pun.

134.37 37 Atypical Activity in a Left Hemisphere Response Selection System in Autism. T. A. Zeffiro*[1], I. Soulières[2] and L. Mottron[2], (1)*Neural Systems Group, Massachussetts General Hospital*, (2)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*

Background: While the most commonly used diagnostic tools for assessing autism emphasize social and language abilities, they generally do not explicitly emphasize motor control skills beyond the assessment of orienting, stereotyped and repetitive movements. This same overall emphasis is reflected in many behavioral studies of autism that report, within a context of developmental milestones in typically developing controls, that differences in basic motor skills are unremarkable compared to atypical linguistic or social skills. Nevertheless, growing evidence demonstrates that autistics experience a range of difficulties in sensorimotor skill acquisition, manifest as dyspraxia, oromotor problems, atypical or absent speech, and difficulty in action imitation. While these atypicalities in complex movement are common, their neural mechanisms are poorly understood.

Objectives: Although complex movement differences can arise from many potential sources, our goal was to explore the hypothesis that the neural systems controlling response selection are differentially engaged in the context of tasks that require selection of one from a range of possible actions. Selection for action has been described as a preferential left hemisphere function involving dorsolateral prefrontal, lateral premotor and posterior parietal cortices.

Methods: We explored the neural systems for action planning in autistics and a matched comparison group using a response selection task, a well-documented method for assessing motor planning operating in the service of voluntary action. A sample of 15 autistic and 17 non-autistic participants, matched on age, sex, IQ and manual preference performed a response selection task that required discrete movements of individual fingers of either the right or left hand to be made in response to one of eight possible visual patterns. Task-related regional patterns of neural activity were estimated using functional MRI.

Results: Although the participants' response time and accuracy did not differ between the autistic and non-autistic groups, greater task-related activity was observed in the non-autistic group in a set of left hemisphere regions associated with visuomotor planning, including posterior parietal cortex, dorsolateral prefrontal cortex, and lateral premotor cortex ($p<0.001$ FWE corrected). In addition, greater bilateral activity was seen in inferotemporal cortex in the non-autistic group. In contrast, greater task-related activity was

observed in the autistic group in regions more closely associated with the execution aspects of movement, including primary motor cortex, the thalamus, putamen and cerebellar cortex.

Conclusions: A group of autistics, not selected on the basis of their motor capabilities, demonstrate clear differences in the cortical mechanisms responsible for visuomotor action planning during a task involving selection of one of multiple possible responses. This differential engagement of a left hemisphere perception-action circuit, observed during performance of a relatively simple visuomotor task, may reflect a more general neural resource limitation encountered by autistics when planning more complex movements. In the context of the higher planning demands associated with complex actions, such as imitation and speech, this resource limitation might lead to easily observable performance differences.

134.38 38 Mirror Neuron System Activation in Autism in Reponse to Transitive and Intransitive Actions. C. Colombi*[1], C. D. Saron[2], M. Beransky[2], Y. Takarae[3], G. Vivanti[4], A. Nadig[5], S. M. Rivera[2], Z. Champion-Fritz[6], S. Ozonoff[4] and S. J. Rogers[7], (1)*University of Michigan*, (2)*University of California at Davis*, (3)*Center for Mind and Brain, UC Davis*, (4)*M.I.N.D. Institute, University of California at Davis Medical Center*, (5)*McGill University*, (6)*UC Davis*, (7)*M.I.N.D. Institute, University of California at Davis*

Background: An apparent conflict is present in current thinking about the role of Mirror Neuron System (MNS) functioning in autism. The conflict involves findings that suggest a global MNS abnormality in autism, and findings that suggest there is preserved MNS functioning based on evidence of understanding of other's actions and intentions in ASD, which stimulates MNS in animals.

Objectives: The goal of this study was to examine mu wave suppression through EEG recording (power in the 8-13Hz band recorded over motor cortex), as an index of MNS activation, to the observation of actions on objects (transitive actions) and body movements (intransitive actions) in children with autism.

Methods: Participants in the current study were 9 children and adolescents with high-functioning autism (8 male, 1 female) between the ages of 9 and 16 years, and 9 children and adolescents with typical development matched on chronological age, language level, Performance IQ, and gender proportion. Continuous EEG was acquired from a customized Falk Minow cap with spherical 124 equidistant scalp electrodes arrangement using a 140 channel Neuroscan Synamps2 system and digitized at 1 kHz while participants were viewing videos of transitive actions involving action and intention understanding and intransitive actions. The experiment was run in 4 blocks of 50 stimuli each with stimulus type randomized. Each video segment was followed by a randomized intertrial interval of 4-7 seconds to prevent anticipation of the stimuli.

Results: When presented with transitive actions children with autism showed mu suppression similar to the control group in both the central and the parietal areas. However, they showed larger suppression to the presentation of intransitive actions in both the central and the parietal areas. Only typical children showed larger mu suppression in the transitive condition in comparison to the intransitive condition. Neither group showed mu suppression in the occipital area.

Conclusions: As predicted, the autism group demonstrated typical mu wave suppression during the observation of transitive actions, a finding that is not explained by the hypothesis of a global MNS dysfunction in autism. The abnormal pattern identified in autism did not reside in a lack of activation but rather in an excess, as shown by larger mu suppression during the presentation of intransitive actions, and a lack of modulation across functions (transitive vs. intransitive), as shown by similar suppression between the presentation of transitive and intransitive actions in autism.

134.39 39 Neural Responsivity to Social Rewards and Mirror Neuron System Activity in Children with and without Autism. A. A. Scott*, S. Bookheimer and M. Dapretto, *University of California, Los Angeles*

Background:

The social motivation hypothesis posits that children with autism spend less time attending to faces and other social stimuli, thus leading to a cascade of negative consequences for the development of social cognition (Dawson et al., 1998; Grelotti et al., 2002). This reduced social motivation is thought to result from a failure to attach a reward value to social stimuli early in development. It has also been proposed that a dysfunctional 'mirror neuron system' (MNS) may give rise to the social impairments that are

characteristic of autism (Ramachandran, 2000). The MNS is thought to constitute a neural substrate for automatically understanding others via a simulation mechanism (Rizzolatti & Fabbri-Destro, 2008). The normal functioning of this system may code the 'like me' analogy between self and others (Gallese, 2003) perhaps contributing to the attentional biases toward social stimuli observed during typical development. MNS abnormalities in autism may alter this developmental trajectory as children with autism may not find social stimuli rewarding if they fail to grasp this self/other equivalence which is fundamental for the development of social cognition (Meltzoff, 2007).
Objectives:

The aim of this study was to examine the relationship between reward-related activity in the ventral striatum (VS) and activity in frontal regions such as the inferior frontal gyrus (IFG) during a socially rewarded learning task in children with and without autism spectrum disorders (ASD).
Methods:

16 boys with ASD (12.4 + 2.14 years) and 16 age- and IQ-matched typically developing (TD) boys were scanned during a socially rewarded implicit learning task. Region-of-interest (ROI) analyses were conducted within the right pars opercularis (PrOp) of the IFG and a functionally defined ROI within the VS. Within-group bivariate correlations were conducted on percent signal change within the PrOp and VS during social feedback events. A multiple linear regression on PrOp activity across groups was also conducted.
Results:

We found significant positive correlations between activity in the VS and activity in the right PrOp (BA 44) for TD children. Specifically, we found that VS response to positive social feedback significantly correlated with both positive ($r = 0.824$, $p < 0.001$) and negative ($r = 0.714$, $p < 0.001$) emotional facial feedback compared to rest, but not with neutral expression positive feedback compared to rest (TD: $r = -0.31$, $p = 0.245$; ASD: $r = -0.21$, $p = 0.435$).No significant correlations for these two ROIs were observed within the ASD group. A multiple linear regression on PrOp activity with group, VS activity and group X VS interaction ($F(3, 28) = 8.362$, $p < 0.001$) revealed a significant interaction effect ($b = 0.88$; $t = 2.17$, $p < 0.05$).
Conclusions:

We found evidence of strong functional connectivity between the right pars opercularis of the IFG and reward-related responses in VS in TD children for emotional social feedback. No such correlations were observed in children with ASD. These findings support the social motivation hypothesis and provide evidence linking MNS dysfunction in autism to reward circuitry abnormalities in response to social stimuli.

134.40 40 fMRI Investigation of Sustained Attention and Sensorimotor Synchronization in Children and Adolescents with Autistic Spectrum Disorder. C. Murphy*[1], A. Christakou[1], E. Daly[2], P. Johnston[1], D. Spain[1], D. Murphy[1], K. Rubia[1] and M. R. C. AIMS Consortium[3], (1)*King's College London, Institute of Psychiatry*, (2)*Institute of Psychiatry, King's College London*, (3)*Institute of Psychiatry, London; University of Oxford; University of Cambridge, United Kingdom*

Background: There is evidence from neuropsychological studies that people with autistic spectrum disorder (ASD) have deficits in sustained attention and sensorimotor timing. However, nothing is known of the underlying neurofunctional substrates of these deficits in children or adults with ASD. We used functional magnetic resonance imaging to compare brain activation in children and adolescents with ASD with that of healthy children and adolescents during performance on a parametric vigilance task that measured sustained attention and sensorimotor synchronization. We hypothesised that children and adolescents with ASD would show reduced brain activation in fronto-striato-temporo-parietal neurofunctional networks of sustained attention and in sensorimotor brain regions in relation to sensorimotor synchronisation.

Objectives:

To investigate brain function in children and adolescents with ASD and healthy Controls during a task that measures sustained attention and sensorimotor timing.

Methods:

28 children and adolescents (11-18 years old) with ASD and 16 age and IQ matched child and adolescent controls completed an event-related parametric Psychomotor Vigilance Task with different temporal delay conditions on a 3T

magnetic resonance imaging (MRI) scanner. All participants were male, right-handed, with an IQ >70. All individuals with ASD met algorithm cut-offs for autism on both the ADI & ADOS. The task requires a motor response to a visual stimulus that appears under qualitatively and quantitatively different delay conditions: 1) long, unpredictable delays of 2s, 5s and 8s and 2) one short predictable delay period of 500ms. Long unpredictable delays have a higher load on sustained attention, while short predictable delays in the milliseconds range are known to trigger sensorimotor synchronisation. Data were analysed using non-parametric image analysis (XBAM).

Results:

Children and adolescents with ASD compared to healthy controls were slower in their reaction times to the 3 unpredictable long delays, but showed no differences in their reaction times to the short delay of 500ms. The fMRI contrasts between all three unpredictable long delays (2s,5s,8s) compared to the predictable short delay showed reduced brain activation in children and adolescents with ASD compared to healthy controls in a right hemispheric sustained attention network of ventrolateral prefrontal cortex, superior temporal lobe, putamen, thalamus and anterior and posterior cingulate. Furthermore, brain dysfunctions became progressively more extensive and bilateral with increasing temporal delay (from 2s to 8s). For the contrast of the short, sensorimotor condition, with long delays, children and adolescents with ASD showed reduced activation in the cerebellum, known to be important for motor timing, and in posterior cingulate and precuneus, presumably related to visual-spatial attention.

Conclusions:

Results suggest that children and adolescents with ASD have extensive abnormalities in fronto-striato-thalamo-temporal networks of sustained attention that increase with increasing attention load, as well as in cerebello-cingulate posterior regions for sensorimotor timing. It is possible that the extensive brain differences observed during sustained attention to temporally unpredictable events relate to the need for 'sameness' displayed by some individuals with ASD.

134.41 41 Response Monitoring on a Face Processing Task and Its Relation to the ERN. C. Hileman*[1], C. Schwartz[2], M. Jaime[1], L. C. Newell[3], P. C. Mundy[4] and H. A. Henderson[1], (1)*University of Miami*, (2)*Yale University*, (3)*Indiana University of Pennsylvania*, (4)*UC Davis*

Background:

Individuals with High-Functioning Autism (HFA) have difficulty with executive functioning skills, including response monitoring.

Objectives:

1) To compare HFA and control participants on behavioral indices of response monitoring during a face processing task.

2) To examine the relation between response monitoring on a face processing task and a neurophysiological index of response monitoring, the Error-Related Negativity (ERN).

Methods:

Twenty children with HFA and 16 children with typical development participated in this study. Participants were presented with a series of upright and inverted faces that were revealed in piecemeal. Participants were instructed to guess the affect of the face as quickly and accurately as possible. After the whole face was revealed, participants could change their original affect selection. The two dependent variables of interest were: 1) percentage of trials in which the original affect selection was correct and 2) percentage of trials in which the participant correctly kept the original affect or correctly selected a new affect. EEG data were collected using Lycra stretch Electrocaps as participants completed a modified Flanker task. Participants were instructed to push a button to identify the direction of the middle arrow on compatible (<<<<< or >>>>>) and incompatible (<<< or >>>) trials. ERN was quantified as the maximum negative peak within 150 ms of the error response. Data were analyzed from site Fz.

Results:

There was an interaction between diagnostic group and orientation on original affect selection, $F(1, 32) = 4.61$, $p = 0.04$, $\eta^2_p = 0.13$. Post hoc analyses revealed that participants with autism were marginally more accurate on selecting affect for inverted faces than control participants, $F(1,$

32) = 3.73, p = 0.06, η^2_p = 0.10. There was also an interaction between diagnostic group and face orientation on the decision to keep/change the affect, $F(1, 32) = 4.05$, p = 0.05, η^2_p = 0.11. Post hoc analyses revealed that control participants made better decisions for upright faces than participants with autism, $F(1, 32) = 5.85$, p = 0.02, η^2_p = 0.16.

A regression was performed with age, diagnostic group, and ERN amplitude as predictors of a composite score of the two face processing variables. Age was a significant predictor of face processing, $B = 0.46$, $t(32) = 3.15$, $p < 0.01$, such that older individuals performed better on the task. Over and above the effects of age, ERN amplitude significantly predicted face processing performance, $B = -0.31$, $t(32) = -2.16$, $p = 0.04$, such that individuals with a higher ERN amplitude had better face processing.

Conclusions:

Consistent with the literature, individuals with autism didn't show the typical advantage for processing upright faces and disadvantage for processing inverted faces. Of particular interest, individuals, regardless of diagnostic group, with heightened error-monitoring on a non-social, Flanker task were better at error-monitoring on a social, face processing task. Response monitoring may be a helpful venue for intervention in autism, as it appears to be an integral component of complex social information processing.

134.42 42 A Mu Rhythm View of Neurofeedback Training Effects of Face Processing Impairments in Autism. J. M. Bai*[1], O. R. Aragon[2], A. Moore[3], H. A. Pelton[3], A. Anaya[3] and J. A. Pineda[3], (1)*University of Illinois at Urbana-Champaign and University of California, San Diego*, (2)*California State University at San Marcos*, (3)*University of California, San Diego*

Background: Face processing plays an important role in understanding nonverbal cues in everyday social interactions. Research has shown deficits for those with autism spectrum disorder (ASD) in the perception of faces and reduced activation in the social brain, including the mirror neuron system (MNS). Previous studies have indicated that MNS activity could be assessed through power suppression of mu rhythms recorded over the sensorimotor cortex.

Objectives: The current study monitored MNS activity during face processing through mu suppression before and after neurofeedback training (NFT). NFT is a learning methodology that involves operant conditioning of EEG frequency bands, including the mu rhythm. It has been used for modifying cortical resonances and behavior through activity-dependent brain reorganization.

Methods: High functioning ASD children, along with matched, typically developing (TD) children were exposed to 20 weeks of NFT before and after exposure to a 1-back memory paradigm using static faces (angry, disgusted and happy faces). We hypothesized that modifying the dynamics associated with mu rhythm leads to activity-dependent brain reorganization and therefore normalization of behavioral responses, including responses to emotional faces.

Results: Both the ASD and TD groups learned to modulate mu power across training sessions. Furthermore, the ASD group showed significant improvement in behavior as assessed by the Autism Treatment Evaluation Checklist (ATEC) after 20 weeks of training. Additionally, this group showed significant mu suppression while observing hand movement following training. This was not shown prior to training.
The TD group showed similar absolute mu power over both hemispheres during building observation (baseline condition). In contrast, the ASD group showed higher absolute mu power on the right compared to the left hemisphere before training. Following training, this lateralization in the ASD group disappeared. Moreover, the TD group showed significant mu suppression over the right hemisphere to the presentation of disgusted and happy faces. However, there was no significant mu suppression in the ASD group during any conditions before or after training. Analysis of absolute mu power showed a highly negative correlation with age in the TD group. In the ASD group, no such relationship was observed (except for over the right hemisphere in the disgusted face condition) before training. However, after NFT, mu power over the right hemisphere displayed a negative correlation with age during face observation, similar to that seen in TD children.

Conclusions: The behavioral results and the mu suppression findings confirm that NFT contributes positively in children with ASD as has been shown in previous reports. However, during face

processing, mu suppression showed no improvement following training. One possible explanation is that the brain area to which NFT mainly applied was the hand area in the right hemisphere. This region may not be sufficient to influence the whole neuronal circuit responsible for face processing. According to the findings from absolute mu power comparison, the right hemisphere became more TD-like in the ASD children following training.

134.43 43 Mapping the Developmental Trajectory of Audio-Visual Integration Using High-Density Electrophysiology. S. Molholm*[1], A. B. Brandwein[1], H. Gomes[2] and J. J. Foxe[2], (1)*The Children's Research Unit (CRU), Program in Cognitive Neuroscience,City College of New York*, (2)*City College of New York*

Background: Many individuals with autism spectrum disorders (ASD) find aspects of the "typical" sensory environment overwhelming. One explanation put forth is that individuals with ASD do not integrate inputs from the various sensory systems (sight, touch, hearing) into meaningful and manageable units, and that this contributes to sensory sensitivities among other perceptual and cognitive sequelae. However there is little empirical research to date that directly tests the integrity of multisensory processing. Objectives: The overarching goal is to establish whether multisensory deficits are present in children with ASD and to characterize the neurophysiological basis of these deficits. Here we use high-density electrical mapping to map the developmental trajectory of basic auditory-visual integration in typically developing children from ages 6 to 17 (N=51). This will serve as a baseline against which to compare multisensory integration in individuals with autism. Data from a group of children with ASD from a more restricted age-range is also examined.
Methods: High-density electrophysiological recordings were made while participants engaged in a simple reaction-time task in which they responded to the occurrence of an auditory, visual, or auditory-visual stimulus. The three stimulus types were presented in an unpredictable randomized order. To assess multisensory interactions, electrophysiological responses (ERPs) to the auditory-alone condition and the visual-alone condition were summed for each participant and compared to the response to the stimulus condition in which the stimuli were presented together (sum versus simultaneous). Data from typically developing children were divided into three age groups to begin to map the developmental trajectory of basic multisensory integration for auditory and visual stimuli. Data from a smaller group of children with ASD were compared to age and IQ matched controls.
Results: Analysis of the data from the typically developing children indicates that there are developmental changes in how the brain integrates simple auditory and visual inputs over the course of childhood. Earlier multisensory interactions were seen in the younger cohorts of children compared to the oldest cohort of children (~100 ms post stimulus onset), whereas later multisensory interactions were more prominent in the older groups. Behaviorally, multisensory integration was signified by violation of the race model. Race model violation was seen to a greater extent in older children compared to younger children, with no evidence of race model violation in the youngest group. Preliminary analysis of data from the ASD group suggests differences in auditory-visual integration compared to an age and IQ matched group of TD children.
Conclusions: Mapping the developmental trajectory of multisensory integration is essential to testing the integrity of these processes in clinical groups such as ASD. Here we use electrophysiology to show that multisensory integration is modified over the course of childhood. Behavioral data from our laboratory on higher order multisensory integration indicate that such malleability is absolutely key to the optimized use of multisensory inputs in perception. Our findings also point to clear differences between multisensory integration in TD children and children with ASD. Continuing work in our laboratory will determine the developmental course of simple auditory-visual integration in this group.

134.44 44 Subphenotyping of Autism Spectrum Disorders Using Auditory Event-Related Potentials. L. M. Marcelino*[1], M. Beransky[1], C. Colombi[2], T. Riggins[3], D. M. Horton[1], L. Deprey[4], T. Kenet[5], S. J. Rogers[6], S. M. Rivera[1] and C. D. Saron[1], (1)*University of California at Davis*, (2)*UMACC*, (3)*University of Maryland*, (4)*UC Davis Medical Center*, (5)*Massachusetts General Hospital*, (6)*M.I.N.D. Institute, University of California at Davis*

Background: Unusual sensory-related behaviors, particularly in response to sound and touch, are associated with the phenotype of autism spectrum disorders (ASD). However, not all children diagnosed with autism exhibit this behavioral profile, and among those who do there may be

sensitivity to relatively weak stimulation or tolerance of strong sensory input.

Objectives: In this study, part of a larger, on-going project to identify autism subphenotypes (The Autism Phenome Project), we sought to identify electrophysiological markers of sensory processing subphenotypes. Our approach was to examine the electrocortical response amplitude recorded to stimuli of increasing loudness. A critical feature of this approach was the development of procedures that yielded robust data from individual very young participants with ASD.

Methods: 60-channel event-related potentials (ERPs) were elicited by randomly presented 50, 60, 70, and 80 dB 50 ms complex tones via headphones from 30 typically developing (TD) toddlers and 30 children diagnosed with ASD. Diagnostic criteria were based on ADOS, ADI-R, DSM-IV and clinical observation. All children (age 2.5 - 4 yrs.) were judged to have clinically normal hearing. ~1000 stimuli with inter-stimulus intervals of 1-2 s were presented as children passively listened to the stimuli and watched a quiet video of their choice. ERPs were derived separately for each intensity. Data analyses included examination of all-waveform overlays, animations of scalp current density topography and derivation of Laplacian waveforms from identified scalp current foci.

Results: For all children, clearly defined auditory ERPs were obtained to at least one intensity level. TD children, compared with children with ASD, generally had more well-defined ERPs to the lower intensity levels and showed a pattern of graded responses with larger cortical activity evoked by louder stimuli. The pattern for children with ASD was much more variable. However, four distinct loudness dependency response profiles were identifiable: 1) a pattern that resembled the typical response of increasing ERP amplitude with increasing stimulus intensity (N=12); 2) a pattern of little variation between intensity levels (Min-diff) (N=6); 3) a pattern of increasing response amplitude that included secondary or "echo" cortical activations (N=7); and 4) a striking pattern of response amplitude *reversal* with the largest responses seen to 50 dB stimuli, with decreasing response amplitude to sounds of increasing loudness. (N=5). The groups differed by age, with the inverse group younger than the echo and Min-dif groups (38 mo vs. 45 mo). Initial examination of neuropsychological data associated with these subgroups, analyzed with age as a covariate, show no difference in DQ scores (Mullens), nor overall ADOS scores. However, ADOS behavioral subscores for the Inverse group were significantly lower than for Echo and TD-like groups and marginally lower than the Min-diff group. The Min-diff group was significantly more impaired on the ADI-R behavioral subscale than each other group.

Conclusions: These data suggest that there are distinct electrophysiological sensory response profiles for subgroups of children with ASD that may account for the observed phenotype of atypical reactions to sounds in some children, and which bear relation with other phenotypic measures.

134.45 45 Electrophysiological Investigation of Auditory Processing in Infants at Risk for Autism Spectrum Disorders or Language Impairment. T. Augenstein*[1], V. Vogel-Farley[1], C. A. Nelson[1], H. Tager-Flusberg[2], L. M. Casner[3] and L. Kasparian[2], (1)*Children's Hospital Boston*, (2)*Boston University School of Medicine*, (3)*Boston University*

Background:
Recent research has highlighted the potential overlap between autism spectrum disorders (ASD) and specific language impairment (SLI) populations which note a significant proportion of first-degree relatives of autism probands have language-related learning disabilities, including SLI, and in a large epidemiological sample, siblings of SLI probands found an elevated risk of ASD. Behavioral studies of children with autism have highlighted a subgroup of verbal children with autism who have deficits in language that mirror those seen in SLI. There are also parallels between ASD and SLI at the neurobiological level with similar patterns of reversed asymmetry in inferior frontal cortex of older children as well as increased brain and white matter volumes. Because the few studies that have directly compared ASD and SLI have all been conducted with older children, it is not known whether there is overlap in the earliest manifestations for each of these disorders in specific symptoms or developmental timing.
Objectives:
This project's objective is to investigate the emergence of neural differences in key aspects of language and social-communicative development during the period between 6 and 12 months (a

significant developmental window during which a number of critically important changes in language and social engagement emerge in typically developing infants) in infants who later go on to show signs of language impairment or ASD the.
Methods:
In the current longitudinal project we are employing high-density event-related potentials (ERPs) tasks to examine auditory processing at 6, 9 and 12-months of age. This study compares three groups of infants: (1) infants at risk for ASD (HRA), (2) infants at risk for SLI (HRL) and (3) low risk infants (LRC). This paradigm was based on a paradigm developed by Rivera-Glaxiola et al. (2005). It was selected because it can be used to chart developmental changes in speech perception in the first year of life and is sensitive to interesting individual differences that predict later language outcomes.
Results:
On the longitudinal data we have collected to date we conducted statistical analyses that were focused, preliminary analyses on the P1 and N250 components, collected from left and right hemisphere fronto-temporal leads, for the auditory stimuli. At 6 months for both components there were marginally significant group x hemisphere effects (e.g., P1 peak amplitude, ($F(1, 23) = 2.19$, $p = .10$). No effects were significant at 12 months, perhaps because of heterogeneity among both groups of infants.
Conclusions:
These pilot data suggest that compared to the LRC in both the HRA and HRL groups there is less asymmetry in response to speech sounds. These findings are consistent with neuroimaging studies of older children with these disorders and their family members. This portion of the larger research program will address more directly the shared and unshared characteristics of these disorders by comparing the early developmental patterns across language and social domains in infants at risk for these disorders using a combination of developmentally sensitive behavioral and neurophysiological measures.

134.46 46 Task-Evoked Pupillary Response to Social Stimuli: Hypoactivation in Autism. J. E. Bedford*[1], J. T. Elison[2], H. F. Levin[3], J. Piven[1] and J. Bodfish[2], (1)*University of North Carolina*, (2)*University of North Carolina at Chapel Hill*, (3)*Guilford College*

Background: Previous research has demonstrated that individuals with autism spectrum disorders (ASD) present difficulties with attentional disengagement. Such perseverative attention may contribute to clinical symptoms of autism such as relative differences in sensitivity to social versus nonsocial sources of information. A marker of "attentional load," or the degree of attentional resources allocated to a particular visual stimulus, is provided by the magnitude of changes in pupillary diameter. The present study investigated task-evoked pupillary responses (TEPR) in children with ASD when disengaging from social and nonsocial stimuli to determine whether allocation of attentional resources to social stimuli was decreased, possibly contributing to patterns of atypical social information processing.

Objectives: To assess the TEPR amplitude, a marker of attentional activation, when children with ASD and typically developing children (TYP) disengage from social and nonsocial stimuli.

Methods: In this study, 20 school age children with ASD (mean age = 145 months, *SD* = 24) and 22 age and IQ matched TYP children (mean age = 158 months, *SD* = 23) completed a modified gap-overlap task. The task presented a central social or nonsocial image of similar size and luminance, followed by a lateral nonsocial image. In the overlap condition, a lateral target appeared while children fixated on the central stimulus, requiring them to first disengage visual attention before reorienting to the periphery. For each of 40 overlap trials, pupillary diameter was examined at four separate epochs of 400 ms duration: (1) before and (2) after the onset of the central stimulus and (3) before and (4) after the participant disengaged and shifted attention to the lateral stimulus. Pupil diameter was measured with a Tobii 1750 eye tracker at a sampling rate of 50 Hz. Trials were deemed valid if a clear saccade from the central stimulus to the peripheral target was recorded between 80 and 1000 ms after the onset of the lateral stimulus. Diameter changes were calculated by pre-trial baseline subtraction to account for dark adaptation, accommodation, and fatigue.

Results: The two groups did not differ in their TEPR to the onset of either type of trial. The TYP group exhibited a pupillary dilation during disengagement from social stimuli. This differed significantly ($p < .01$) from the pupillary constriction shown by the ASD group in both social and nonsocial disengagement conditions

and by the TD group in the nonsocial disengagement condition.

Conclusions: As measured by pupillary response, children with ASD failed to allocate attentional resources to disengage from social stimuli at the same rate as the TYP children. Hypoactivation to social stimuli may be one component process that contributes to deficits in orienting to salient social information in autism. Activation to nonsocial information may be a relative strength in autism and when paired with deficient activation to social information, may result in an overall pattern of increased attention to and experience with the nonsocial world.

134.47 47 Enviromental Risk Factors and ASD: Case-Control Study in Spain. C. Martín-Arribas*[1], P. Garcia Primo[1], E. Garcia Andrés[1], M. Morueco Alonso[2], J. Hernandez Rodriguez[3], M. M. Herraez García[4], L. Herraez García[4], V. Martin[5], Z. Guisuraga[4], J. Santos Borbujo[4], B. Mongil[4], C. Domínguez[4], P. Palomino[6], R. Canal-Bedia[5], R. Vidal[6], S. Diez[7] and M. Posada de la Paz[1], (1)*Carlos III Health Institute. Rare Diseases Research Institute.*, (2)*Fundacion Gaspar Hauser*, (3)*Universidad Autonoma de Madrid*, (4)*UNIVERSIDAD DE SALAMANCA*, (5)*Universidad de Salamanca*, (6)*Fundacion Jimenez Díaz*, (7)*ICTJA-CSIC Institut Ciencies de la Terra*

Background: The causes and contributing factors for autism are poorly understood and the mechanisms of pathogenesis have yet to be delineated. There is a growing literature on exposure to environmental agents, genetic factors as well as interactions between them and genetic predisposition as potential causes of autism.
In September 2005 it began a pilot ASD screening program in Spain (Ferrari MJ et al, IMFAR 2008). One year later parents of children diagnosed with ASD through this program were invited to be part of a case-control study.
Objectives: To explore environmental risk factors potentially associated with the development of these disorders as well as the possible role of the immune system in the etiology of autism.
Methods: Design: Case-control study. ASD cases with two controls for each case were matched by age, sex and geographical residential area during pregnancy and child early life. All sample subjects must be diagnosed by expert clinicians trough the same standarized diagnosis tests such as ADOS-G, Vineland, Merrill Palmer-R, as well as clinical judgement based on F.84 DSM- IV TR.
Cases: All children aged from 18 to 32 months old with an ASD diagnosis from the screening programs, centres of early intervention and from ASD associations in Spain.
Controls: Children diagnosed with other developmental disorder (ODD) (Language Impairment, Global Developmental Delay, etc) and children with typical development (TD).
Variables: Parents Medical History, Lifestyle and records signs as well as parents Pre- peri- and post- natal residential and working environmental exposure data collected through questionnaires.
Immunological tests: IgG, IgA and IgM levels in serum, antibodies against neuronal antigens and glangliosides and total mercury levels (Hg) through blood and hair samples.
Results: Questionnaires on environmental risk factors have been developed as well as the protocols to gather and analyse the biologic samples in order to standardize the process. At the same time, diagnosis in the three sample groups has been confirmed.
The study is in the first phases but they have been already recruited more than 50 children. Blood and hair samples and exposures data have been collected from 39 children (15 PDD, 9 ODD, and 15 TD). Initial analyses do not indicate significant differences on Hg levels.
High values of IgG have been observed in some of them. Additionally, the study of antibodies against neuronal antigens and gangliosides has showed reactivity against two gangliosides (GM1 and GM2).These results must be confirmed through of indirect immunofluorescence test (IIFT).
Conclusions: This study is the only case-control study on environmental risk factors and autism ongoing in Spain. It seems possible to identify some possible risk factors.

134.48 48 Associations Between Early Measures of Medical Complications and Neurobehavioral Integrity with Later Dimensional Measures of Autism Traits in NICU Infants. I. L. Cohen*[1], B. Z. Karmel[1], J. M. Gardner[1], E. M. Lennon[1], L. D. Swensen[1] and T. Rovito Gomez[2], (1)*NYS Institute for Basic Research in Developmental Disabilities*, (2)*New York State Institute for Basic Research in Developmental Disabilities*

Background:

Autism is a complex disorder of development and represents a subclass of Pervasive Developmental Disorder (PDD). It is crucial to identify early biological and behavioral risk factors for PDD, as well as for its severity, since there is evidence that early intervention is effective in improving long-term outcome, especially among more mildly affected cases. Researchers have attempted to identify early signs by studying "baby sibs" - infant siblings of children with autism (10-fold

increased risk for developing PDD). Another group at risk is infants with obstetrical/neonatal complications (3-4 fold risk).

Objectives:

The Behavioral Assessment and Research group in the Dept. of Psychology at IBR has diagnosed with PDD approximately 1/3 of the 2% suspect cases who had been studied intensively by the Infant Development group. Data will be presented on the behavioral characteristics of this subgroup of PDD, how they compare with typically referred cases, and the relations between early physical and neurobehavioral measures with later dimensional measures of PDD traits and adaptive skills measured at an average age of 4 years.

Methods:

Infants were evaluated in the NICU prior to discharge and followed every 3 months between 1 and 25 months (post term age). Infancy measures included anthropometric measures obtained at birth, measures of degree of neurological insult, and a variety of behavioral and cognitive assessments. Behavioral diagnostic assessments when children were, on average, 4 years of age, included the Autism Diagnostic Observation Schedule-G (ADOS-G), Vineland Adaptive Behavior Scales, and parent and teacher ratings using the PDD Behavior Inventory (PDDBI), an age-standardized dimensional measure of PDD traits.

Results:

Preliminary data suggest moderate to strong associations between birth measures (e.g., body length, birth weight) and neurobehavioral assessments (e.g., atypical looking preferences to higher amounts of stimulation) performed before 12 months of age with later PDDBI domain scores: SENSORY (sensory seeking-type behaviors); SOCIAL DISCREPANCY Composite (a measure of social competence); AUTISM Composite (a measure of autism severity); REPRIT Composite (a measure of classic autism traits); and AWP Composite (a measure of autistic and non-specific behavioral traits).

Conclusions:

NICU infants are at high risk for PDD, in addition to other developmental disabilities. These data indicate that early physical and neurobehavioral measures suggest associations to later PDD traits. The patterns thus far, although specific to these NICU infants, appear to fall between those for CNS-injured and cocaine-exposed infants.

134.49 49 Alterations in Lipid Metabolism and Anti-Oxidant Status as Specific Biomarkers of Autism Plasma. D. B. Goodenowe*[1], E. Pastural[1], Y. Lu[1], W. Jin[1], D. Heath[1], R. Friend-Heath[1], M. Fisk[2] and P. L. Wood[3], (1)*Phenomenome Discoveries*, (2)*Jonty Foundation*, (3)*Phreedom Pharma Inc*

Background: Our initial findings using a Fourier Transform Ion Cyclotron Resonance Mass Spectrometry (FTMS) based comprehensive non-targeted metabolomic platform revealed alterations in the levels of very long chain fatty acid (VLCFA) containing phosphatidylethanolamines (PtdEtn) and in DHA containing plasmalogens (PlsEtn) in autism plasma (unpublished results).

Objectives: To validate and expand these findings, we investigated more thoroughly fatty acid elongation, DHA synthesis, and plasmalogen synthesis using serum from autistic subjects. We measured the plasma levels of ethanolamine phospholipids containing fatty acids ranging from 16 to 40 carbon units and from zero to six double bonds. We also investigated markers of glutathione pathway in order to investigate a possible correlation between lipid metabolism and oxidative stress in autism.

Methods: Three plasma samples from 15 autism subjects and 12 non-autism controls were collected over a 12 month period (six month interval between samplings). Phospholipid and thiol levels were determined by tandem LC-MS/MS analyses using a linear ion trap mass spectrometer (4000 Q TRAP, Applied Biosystems) coupled with an Agilent 1100 LC system.

Results:

Plasma levels of 136 phosphatidyl ethanolamines and 15 ethanolamine plasmalogens were measured and compared to levels observed in non-autistic subjects. The results of these analyses revealed that autistic subjects had increased levels of fatty acid synthesis, elongation, and desaturation products relative to controls. Every non carnitine-supplemented autistic subject exhibited elevated plasma levels ($p<0.05$) of either docosahexaenoic acid containing ethanolamine plasmalogens (DHA-

PlsEtn) or very long chain fatty acid containing phosphatidylethanolamines (VLCFA-PtdEtn), whereas all autistic subjects taking carnitine supplementation had normal levels of DHA metabolites and 2/4 had slightly elevated levels of VLCFA metabolites. Since over half of the ethanolamine phospholipids in the membrane of neurons are plasmalogens and DHA plays an essential role in the membrane biophysical properties, the abnormalities we observed in the non carnitine supplemented autistic subjects are expected to alter neuron plasticity and therefore neurotransmission. An overall increase in plasmalogens (increase in some specific plasmalogens without a decrease in others) can be hypothesized to explain the hypersensitivity frequently observed in autism.

In a second step, we found that all autistic subjects had decreased levels of reduced glutathione (GSH) and metabolic precursors of GSH, regardless of their supplementation status. Basal levels of carnitine and acetyl carnitine were normal in non-supplemented subjects and elevated in carnitine supplemented subjects. The decreased anti-oxidant capacities we observed in all autistic subjects confirm the results reported by other groups and delineate the limitations of carnitine supplementation in autism.

Conclusions:

The serum of autistic subjects displayed markers of increased oxidative stress, in association with a specific phospholipid pattern for the non carnitine supplemented subjects. It is our hypothesis that the phospholipid pattern arises from a chronic exposure to glutamate as we discuss in our second abstract (in Model Systems). These results raise the promising possibility of diagnosing autism by a simple plasma draw.

134.50 50 Diagnosis and Treatment of Catatonia in Autism: Cerebrospinal Fluid Neurotransmitter Findings and Treatment Response; Role for New Therapeutic Options. M. Chez*[1], E. Bell[2], S. J. Spence[3], R. G. Robinson[4] and K. Hyland[5], (1)*Sutter Neuroscience Institute, Sacramento; UC Davis Medical Center*, (2)*Cure Autism Now*, (3)*NIH*, (4)*Descanso Medical Center*, (5)*Medical Neurogenetics*

Background: Patients with autism have been described as developing movement disorders of catatonic type. In addition autism has rarely been associated with central folate deficiency with motor problems in early childhood. Traditional reviews in the literature have not evaluated for possible neurotransmitter problems. Treatments have been limited to either lorazepam or electroconvulsive treatments in the past. We describe the presence of various neurotransmitter abnormalities in 6 patients and their response to folinic acid and/or dopamine replacement therapy.

Objectives:

Patients with autism have been described as developing catatonia but rarely studied for neurotransmitter deficiency. In six cases, lumbar spinal fluid was collected to evaluate the possibility of defective neurotransmitter or folate metabolism. Patients all had normal neuroimaging studies on 1.5 tessla MRI.

Methods: Lumbar cerebrospinal fluid (CSF) was collected under defined conditions from 6 male patients (ages 11,13, 14(2),15, 17 years) with autism and catatonia. Two patients also had brain nuclear medicine SPECT brain scans and all had 1.5 Tesla MRI brain imaging, reported as normal in all patients. CSF was analyzed for neurotransmitter metabolites homovanillic acid (HVA) and 5-hydroxyindoleacetic acid (5-HIAA) and 5-methyltetrahydrofolate (5MTHF) using HPLC and electrochemical detection. Comparison data in other younger non-catatonic autistic children who had CSF data showed no neurotransmitter metabolite abnormality (N=12) and are used as a control group.Treatment outcomes are described using either folinic acid or levodopa/carbidopa.

Results:

Three patients showed low abnormal metabolite levels. The two most severely catatonic patients had low HVA (49;139 reference range 167-563 nmol/l) and low 5-HIAA (34; reference range 67-189 nmol/l) and borderline 5MTHF (44; reference range 40-150 nmol/l). A second patient had a low CSF 5-MTHF level of 29nmol/l. A third patient with dystonic gait onset showed low 5HIAA levels only (65; reference range 67-189 nmol/l). Another 2 patients had high 5-HIAA levels. Treatment with folinic acid at 10-20mg BID led to clinical improvement in 4/6 patients and levodopa/carbidopa supplementation in addition helped 2 patients with low HVA or 5-HIAA.

Conclusions: These patients with autism had late childhood or adolescent regressions with onset of catatonia. The presence of abnormal levels of neurotransmitter metabolites or 5MTHF in 5 of

these patients, together with a clinical response to folinic acid or dopamine replacement therapy, suggests that changes in these areas of metabolism may be frequent in this patient population. Non-catatonic younger children with autism do not have these findings. A larger study is warranted to determine if the appearance of catatonia in individuals with autism may be the clinical manifestation of an underlying developmental or aquired neurotransmitter disorder.

134.51 51 Assessment of a Biomarker of Prenatal Mercury Immunotoxicity: a Cross-Sectional Study. J. F. Nyland*[1], S. B. Wang[2], E. C. O. Santos[3], A. M. Ventura[3], J. M. de Souza[3] and E. K. Silbergeld[2], (1)*University of South Carolina School of Medicine*, (2)*Johns Hopkins Bloomberg School of Public Health*, (3)*Institute Evandro Chagas*

Background: Evaluating the potential impacts of prenatal exposures on the maternal and fetal immune systems (both as a unit and separately) has been hampered by lack of information on the relative contribution of each component to serum biomarkers such as IgG and IgM antibodies. We have examined the effects of prenatal mercury exposures on immune biomarkers in serum prepared from cord blood and maternal blood samples in a population exposed to methylmercury. Mercury is a ubiquitous environmental contaminant with known neurodevelopmental effects at high exposures and its role in the development of autism/autism spectrum disorders remains controversial. Recent studies on the toxic properties of mercury have highlighted the implications at lower exposures particularly on the immune system. Low level prenatal exposure through maternal contaminated fish consumption has the potential to impact the immune system of the fetus, potentially increasing susceptibility to disease. Many studies have been undertaken to identify a reliable biomarker of the immunotoxic effects of mercury. We have previously reported that antigen-specific autoantibodies (anti-nuclear, ANA) may be informative biomarkers of mercury-induced immunotoxicity.

Objectives: In this study, we assessed the effects of prenatal exposure to mercury on total and ANA immunoglobulins in a cross-sectional sample from a prospective mother-infant cohort study in Amazonian Brazil.

Methods: We compared maternal and cord blood mercury and antibody levels with maternal covariates obtained by questionnaire. Serum levels of total immunoglobulin were measured by ELISA and ANA levels by indirect immunofluorescence of serial 2-fold dilutions on HEp-2 slides according to standard clinical methods.

Results: Blood mercury concentrations were higher in cord blood than in maternal blood (geometric mean of mercury in mothers was 6.9 and in cord blood it was 9.6 ug/L). We found that total and ANA IgG, but not IgM, levels were correlated with both maternal and cord blood immunoglobulin. Moreover, total IgG level in cord blood was significantly associated with fetal mercury level. ANA titer in either maternal or cord blood was not significantly associated with either maternal or cord blood mercury levels.

Conclusions: These findings are consistent with research on the ability of IgG, but not IgM, to cross the placenta in the absence of infection and thus indicate that measurements of both immunoglobulins may provide insight on differential responses of fetuses and mothers to a toxicant that crosses the placental barrier. These data provide further evidence for the immunotoxicity of mercury at low dose, and the first evidence for such effects during prenatal development. This research was supported by grants from the National Institutes of Environmental Health Sciences K99 ES015426 (JFN) and the Johns Hopkins University Center for a Livable Future (JFN).

134.52 52 Parental Perception of the Causes of Autism Spectrum Disorders with An Emphasis on Genetic Factors. V. Chirdkiatgumchai*, N. Ruangdaraganon, R. Roongpraiwan, T. Sombuntham, P. Rojmahamongkol and R. Prasertchai, *Faculty of Medicine, Ramathibodi Hospital, Mahidol University*

Background: More than 90% of cases of autism spectrum disorders (ASDs) are idiopathic and are multi-factorial in etiology. To provide better genetic counseling, a clear understanding of parental perspectives on genetics and multi-factorial as an etiologic factor of ASDs is necessary.

Objectives: The aims of this study were: 1. to examine parental perception of the causes of ASDs with an emphasis on genetic factors 2. to identify factors associated with parental perception of the contribution of genetics as a cause of ASDs, and factors associated with the

appropriate perception of multi-factorial inheritance of ASDs.

Methods: The study population consists of parents with at least one child diagnosed with ASD recruited from the Child Development Clinic and the Child and Adolescent Psychiatric Clinic at Ramathibodi Hospital. Participants who visited the clinic during January 2006 to December 2007 were contacted either by mail or directly at the time of visit to obtain informed consent. Parents of children with non-idiopathic ASDs including known genetic disorders (e.g. Rett syndrome, fragile X syndrome, tuberous sclerosis) were excluded from the study. From each participating family, only one parent was asked to complete the questionnaire. The questionnaire was divided into 5 parts including participants' demographic data, general knowledge of ASDs, parental perception regarding causes of ASDs, ASDs recurrence risk, and general knowledge of common pediatric diseases with multi-factorial pattern of inheritance.

Results: Participants included 252 parents of children with ASDs. When questioned regarding the cause with more than one response possible, 44.0% (111/252) of respondents cited genetics as a cause, 62.7% (158/252) reported other factors such as maternal stress and toxic substance exposure during pregnancy, child rearing, etc. Of those who cited genetics as a cause, 78.4% (87/111) had the perception of a multi-factorial concept defined as persons who have genes associated with autism but whether or not ASDs is apparent also depends on environmental factors. According to multivariate analysis, positive family history of ASDs and of speech delay, recurrence risk perception, and knowledge of allergic rhinitis (AR) and attention-deficit hyperactivity disorder (ADHD) as genetic diseases were associated with parental perception of genetics as underlying causes of ASDs. Multivariate analysis also revealed that associated factors with appropriate parental perception of multi-factorial inheritance concept of ASDs were positive family history of ASDs, describing correct definition of ASDs, recurrence risk perception, and having knowledge of AR and ADHD as genetic diseases.

Conclusions: Most of parents cited one or more causes to explain ASDs in their child. Less than half of Thai parents cited genetics as a cause of ASDs. For parents who cited genetics, there is tendency for them to have appropriate perception of multi-factorial concept of ASDs.

134.53 53 The Etiology of Social and Nonsocial Components of Autistic Behavior in Young Twins. L. R. Edelson*[1], A. Ronald[2] and K. J. Saudino[1], (1)*Boston University*, (2)*Birkbeck College, University of London*

Background: Autistic symptoms are present in individuals without a diagnosable autism spectrum disorder and show quantitative variation in the general population (Hoekstra et al., 2007). Further, it has been shown that in a general population sample of school-age children, the genetic influences on autistic-like social behaviors are only modestly overlapping with genetic influences on nonsocial symptoms, with most of the factors being specific to either one class of behaviors or the other (Ronald et al., 2005, 2006).

Objectives: The purpose of this study was to explore the etiology of the social and nonsocial components of ASD symptoms in a younger sample of twins, because it is possible that the genetic architecture underlying these behaviors differs across age groups. The age of two is particularly salient because it is frequently acknowledged that this is the age when autism can first be reliably diagnosed (DiCicco-Bloom et al. 2006).

Methods: Participants included 312 same-sex pairs of 2-year-old twins (144 MZ, 168 DZ). Autistic-like behaviors were assessed via parent ratings on the pervasive developmental problems subscale of the CBCL (Achenbach & Rescorla, 2000). This subscale was divided into behaviors that were social in nature (e.g., poor eye-contact and peer relationships) and those that were considered nonsocial (i.e., relating to restrictive/repetitive behaviors and interests). Cholesky bivariate decomposition models were fitted to the data.

Results: Intraclass correlations were stronger for identical than for fraternal twins for both social and nonsocial autistic-like behaviors, suggesting that both categories of behaviors were genetically influenced to some extent. Several Cholesky decomposition models were fitted to the data. The full ACE model accounts for genetic factors, as well as shared- and nonshared environmental influences; reduced versions of this model were also fit, with an AE (genetics and nonshared environment) being the best-fitting model. This

reduced model showed both social and nonsocial ASD behaviors to be influenced by genetic factors (.52 and .47, respectively), but with limited overlap between the two categories of behavior, with only 13% of the variance in nonsocial behaviors explained by common genetic influences from social behaviors. In the full model, which also includes shared environmental influences, this common genetic variance component drops to 5%, with shared environment accounting for an additional 11%.

Conclusions: While both social and nonsocial autistic-like behaviors are highly heritable in 2-year-olds, genetic model-fitting analyses show that distinct genetic factors are influencing each cluster of symptoms with little overlap. These findings are consistent with previous findings in school-age children (Ronald et al., 2005, 2006). The results suggest that social and nonsocial symptoms are inherited to some extent independently; considering them separately might aid future molecular genetics research.

134.54 54 Plasma Oxytocin Variation in Families with Children with Autism Spectrum Disorders. S. Jacob*, C. S. Carter, P. Suppatkul, C. W. Brune, H. Pournajafi-Nazarloo and E. H. Cook, *University of Illinois at Chicago*

Background:

Studies have reported genetic linkage and association with autism for the oxytocin receptor gene (OXTR) within independent samples. Our laboratory found overall association with autism and the rs2254298 single nucleotide polymorphism in OXTR (Jacob et al 2007). Children with autism were reported to have lower average levels of blood oxytocin (OT) in comparison to typically developing children matched for age (Modahl et al 1998). OT blood levels may serve as an intermediate phenotype that will help identify autism related genes.

Objectives:

To utilize enzyme immunoassay (EIA) methods to measure oxytocin in the blood of children with autism spectrum disorder (ASD) and their family members. Examining neurochemical heterogeneity in children with ASDs, will allow us to identify children with or without disruptions in OT and to explore relationships to genetic variation. For clinical phenotype, we focused on non-verbal social communication given previous results in our lab and others (Brune et al 2007, Green et al 2001, Modahl et al 1998).

Methods:

We are investigating a growing sample (age 3 to 50 years) who meet clinical, Autism Diagnostic Interview-Revised (ADI-R), and Autism Diagnostic Observation Schedule (ADOS) criteria for ASD and their families. Children completed extensive diagnostic testing including IQ measures and physical exams. Blood was collected in chilled glass tubes containing disodium EDTA and kept on crushed ice. The samples were centrifuged at 3500 rpm for 10 min in a freezing centrifuge 4 degree C. Plasma samples were divided into storage vials and stored at -80 degree C. OT was measured using the enzyme immunoassay (EIA) kit developed by Assay Designs, Inc. (Ann Arbor, MI). Assay Designs reported cross-reactivity for similar neuropeptides found in mammalian sera at less than 0.001% and a minimum detection limit of 11.7 pg/ml. EIA samples were diluted 8 fold and manufacturer's instructions were followed (Carter et al. 2007). OT values greater than 2 SD from the mean were excluded from descriptive statistics and assays will be re-run. Given OT distribution, we used nonparametric statistics.

Results:

Preliminary results were obtained for 28 probands and their families with EIA. Mean OT from probands was 442 pg/ml (SD=555), from mothers was 409 pg/ml (SD=272), from fathers was 314 pg/ml (SD=99), and from 14 siblings was 204 pg/ml (SD=141). Further analyses and quantification will be required to examine relationships between families and probands versus non-affected siblings. Preliminary results show a positive trend between proband OT levels and ADI-R "failure to use nonverbal communication to regulate social interaction" sub-domain scores (Kendall tau, p=.06). This was the single subdomain examined. Future analyses will examine patterns of OT levels within families and the relationships between phenotype and genotype.

Conclusions:

Preliminary results show that plasma oxytocin measured by EIA show a broad range of values and a skewed distribution. Our goal is to

establish a methodology that will facilitate studying OT as an intermediate phenotype within ASD. This may be correlated with observable behavioral differences in phenotype. It will also allow us to connect phenotypic differences to genetic associations with autism and oxytocin-related genes.

134.55 55 Oxytocin Treatment to Improve Social Cognition in Young People with Autism. A. J. Guastella*[1], S. Einfeld[1], K. M. Gray[2], N. Rinehart[2], T. Lambert[1] and B. J. Tonge[2], (1)*University of Sydney*, (2)*Monash University*

Background: Recent developments in the field of neuroscience suggest the hormone and neuropeptide Oxytocin has a key role in human social behaviour. Laboratory data demonstrates that the administration of Oxytocin Nasal Spray improves face perception, social memory, and performance on empathy tasks in non-clinical samples. Research is now growing to demonstrate a link between oxytocin and some of the social problems found in Autism Spectrum Disorders. Oxytocin may represent a radical new treatment to improve some of the socio-emotional difficulties observed in autistic spectrum populations.

Objectives: The aim of this trial was to conduct a first trial of Oxytocin Nasal Spray to determine its effect on eye gaze, emotion perception and social cognition in Autistic youth.

Methods: In a crossover double blind, randomized controlled trial we gave 20 youth aged between 12 and 20 a single dose of Oxytocin Nasal Spray or a placebo before completing a range of emotion perception, face processing and social cognition tests 45 minutes later.

Results: Complete results of the trial will be presented at the time of presentation showing how Oxytocin Nasal Spray influences social cognition in Autistic youth.

Conclusions: The implications of these results for Oxytocin Nasal Spray as a treatment to enhance social cognition in Autism will be discussed. Recommendations for future research will also be made.

134.56 56 Social Processing in Autism Spectrum Disorder versus Agenesis of the Corpus Callosum. R. Booth*[1] and F. Happé[2], (1)*Institute of Psychiatry, King's College London*, (2)*Institute of Psychiatry, KCL*

Background: Imaging studies in autism have reported a reduction in the size of the corpus callosum, suggesting it is a disorder of connectivity among brain regions, in particular between hemispheres. An interesting group of individuals to compare with autism are those with agenesis of the corpus callosum (AgCC), where the corpus callosum has failed to develop either completely or partially in utero. AgCC is a rare condition, with a recent estimate of 2.6 per 10,000 live births (1.8 per 10,000 for isolated AgCC unaccompanied by additional neurological abnormalities or genetic syndromes). AgCC is associated with a wide range of behavioural and cognitive difficulties from severe to mild learning difficulties or no developmental delay. Recent evidence suggests that even when cognitive or intellectual impairments are not obvious, subtle deficits in socio-communicative functioning may still be present.
Objectives: The aim of this study is to see whether individuals with isolated AgCC share some of the social deficits of individuals with autism spectrum disorder (ASD) due to problems in theory of mind and/or emotion processing. The ultimate aim is to contribute to understanding the brain basis of social comprehension.
Methods: 16 individuals with partial (N = 7) or complete (N = 9) AgCC (aged 6 to 51 years; IQ 69-111) were compared on a battery of tasks assessing social understanding and emotion recognition to 16 individuals with ASD and 16 typically developing controls, matched individually for age, gender and IQ. Where available, information was also collected from parents about participants' social functioning and adaptive abilities.
Results: A subgroup of individuals with AgCC was found to have a cognitive profile characteristic of individuals on the autism spectrum. However, social functioning can be intact in the absence of the corpus callosum: half the individuals with AgCC were unimpaired across tasks of emotion processing and representing the mental states of others.
Conclusions: Individuals with AgCC present a complex picture and the social difficulties encountered in some individuals include a difficulty recognising others' thoughts and feelings. Further studies, including for example DTI, are needed to establish why some individuals with AgCC show ASD-like social impairments while others do not. The present findings, however, with a sample size that is large in the study of AgCC, do suggest that even complete absence of the corpus callosum is not in itself sufficient to cause ASD.

134.57 57 Mommy, My Ear Hurts: Effects of Ear Infections, Antibiotics in Children with Autism. N. Adams* and E. M. Griffith, *University of Alabama at Birmingham*

Background: Autism is a neurodevelopmental disorder characterized by impairments in social interactions, communication skills, and the presence of restrictive and repetitive behaviors. In the search for biological markers for this behaviorally defined disorder, it has been suggested that recurrent Otitis Media or ear infection, (an inflammation of the tympanic membrane treated with antibiotics) may signal a predisposition.

Objectives: The current study is being implemented to explore the previous findings of the possibility of ear infections and antibiotic usage as a potential indicator for autism.

Methods: Archival data consisting of pediatric medical records and scores from the Autism Diagnostic Observation Schedule from patients assessed for an autism diagnosis were analyzed.

Results: : Pearson Chi Square test shall be conducted upon the categorical variables of ear infections (yes vs. no), antibiotic use (0-2 prescriptions vs. more than 2 prescriptions), and group membership (ASD vs. DD). We predict that ear infections and higher antibiotic usage will be more prevalent in those with autism than those with developmental delays. Additionally, a one-way analysis of variance shall be run to determine the categorical variables between ear infections or antibiotic use, and the continuous variable of symptom severity. We hypothesize that high degree of symptom severity will be found in those with ear infections and high antibiotic usage. Conclusions: Previous research has only compared typically developing children against those with autism in examining the relationship between autism and ear infections. With the present study, we hope to find that a significant difference exists between those with autism and those with developmental delays. Furthermore, in undertaking to clarify the relationship between the ear infections and autism, we hope to find an earlier identification date for those with autism.

134.58 58 Characterization of Children with Epilepsy and Autistic Disorder. H. Wood*[1], T. Humphries[2], J. Brian[3] and W. Roberts[2], (1)*University of Toronto and Hospital for Sick Children*, (2)*University of Toronto*, (3)*Hospital for Sick Children & Bloorview Kids Rehab*

Background: The presentation of Autistic Disorder (AD) in individuals with epilepsy is under-acknowledged and poorly understood. Recent research is suggestive of an elevated rate of the behavioural traits representative of AD, and many children with epilepsy may in fact meet the diagnostic criteria for AD (Boel, 2004; Clark et al., 2005; Steffenburg et al., 2003).

Objectives: The present study sought to characterize a group of children presenting with epilepsy and AD, through consideration of both the AD clinical phenotype, seizure history variables, and cognitive, language and adaptive behavioural functioning.

Methods: 23 participants with epilepsy and AD (EPI/AUT group) aged 5 to 12 years were matched (based on age and gender) to 23 participants with epilepsy who were not identified as having AD (EPI group), in order to consider group differences with regard to seizure history. In considering group differences in AD clinical phenotype, the participants composing the EPI/AUT group were matched to 23 participants with AD and not epilepsy (AUT group), and scores on AD diagnostic measures (ADOS and ADI-R) were compared. All three participant groups were compared for differences in cognitive, language, and adaptive functioning. Within group comparisons for gender and AD diagnostic history were considered for the EPI/AUT group.

Results: The EPI group was found to be functioning significantly better than the EPI/AUT and AUT group in terms of cognitive, language and adaptive functioning. No significant differences on these domains were evident between the EPI/AUT and AUT groups. Consideration of seizure history revealed that the EPI/AUT group was significantly more likely to be on antiepileptic drug (AED) polytherapy, to have a younger age of seizure onset, and have a higher seizure frequency when compared to the EPI group. No significant differences in AD symptom expression on diagnostic measures (ADOS and ADI-R) were identified between the EPI/AUT and AUT groups. The duration of autistic regression was found to be significantly longer in the EPI/AUT group compared to the AUT group. AD in the EPI/AUT group was diagnosed at a significantly older age, and group members were significantly less likely to have received AD-specific treatment than the AUT group. It was

found that 60.9% of the participants in the EPI/AUT group had not been diagnosed with AD prior to involvement in the current study, and the reasons for delayed diagnosis remain unclear. Females in the EPI/AUT group were found to have significantly lower verbal intellectual functioning, a younger age of seizure onset, and to be more often treated with AED polytherapy when compared to males.

Conclusions: The success of initiatives to characterize the presentation of epilepsy/AD is important in increasing awareness among healthcare professionals of this comorbidity, so as to facilitate both timely diagnosis and access to appropriate treatment. Results of the current study suggest that although the AD clinical phenotype is similar, a diagnosis of AD is often not made for individuals with epilepsy. Particular seizure history variables and female gender may represent differentiating factors for comorbid epilepsy/AD.

134.59 59 Persistence of the Primitive Visual Rooting Reflex in Subjects with Autism Spectrum Disorders and Intellectual Disability. E. J. Mulder[1], A. de Bildt[1], N. D. J. van Lang[2], S. A. J. de With[1], G. M. Anderson*[3] and R. B. Minderaa[1], (1)*University Medical Center Groningen*, (2)*Leiden University Medical Center / Curium*, (3)*Yale University School of Medicine*

Background: The behavioral abnormalities of the Autism Spectrum Disorders (ASDs) apparently arise from underlying neurobiological mechanisms that are largely genetically determined. Individuals meeting diagnostic criteria for autism appear to form a behaviorally, neurobiologically and genetically heterogeneous group. Examining specific behavioral components or dimensions in ASD individuals might provide a route to understanding the ASDs. ASD-related phenomena that are not seen at greater than population base rates in family members (such as intellectual disability and seizures) are of particular interest. These "emergenic" phenomena appear to arise from a combination of abnormalities in affected individuals, may have a large influence on behavioral and neurobiological expression, and might be particularly sensitive to early intervention. Among potentially emergenic phenomena are persistent primitive reflexes, including the visual rooting reflex (VRR).

Objectives: We wished to characterize the persistence of the Visual Rooting Reflex (VRR) in a large group of individuals with ASD and Intellectual Disability (ASD+ID) and in a contrast group of subjects with ID only. Specifically, we sought to determine the occurrence (rates) of persistent VRR in the ASD and ID groups, and to examine whether a persistent VRR was associated with severity of domain impairment and with specific behavioral/demographic aspects.

Methods: Presence of a VRR was evaluated in 155 ASD+ID subjects (IQ < 70) and in 65 subjects with ID only. All subjects were ascertained through a population-based epidemiological study on the prevalence of ASD+ID in a Dutch province. Subjects were assessed with the ADI-R, ADOS, Vineland Adaptive Behavior Scales, and standardized intelligence tests. Mean(±SD) ages in the ASD+ID and ID groups were 11.5 yrs±4.0 and 12.3±4.0, respectively; and mean IQs were 39±18 and 45±15, respectively. Presence of the VRR was rated by two trained raters with a kappa of .93 (N=24). Possible associations with age, sex, IQ and behavioral measures were examined. VRR occurrence in autistic disorder (N=95) and PDD-NOS (N=60) subgroups was also examined.

Results: The proportion of subjects with a positive VRR was significantly higher in the ASD+ID group compared to the ID group (52% versus 29%, p=0.002). The occurrence of VRR in the Autistic Disorder+ID subgroup (63%, N=95) was greater than in the PDD-NOS subgroup (44%, N=60; p=0.02). ASD+ID subjects with a positive VRR had significantly lower IQ's; in both groups, lower IQ was associated with a positive VRR. Severity of impairment in the social interaction domain was significantly greater in ASD+ID subjects with a positive VRR compared to those without. Age and sex did not significantly affect the presence of the VRR.

Conclusions: Persistence of the visual rooting reflex (VRR) was significantly and strongly associated with the presence of ASD, lower cognitive functioning and greater social interaction domain impairment. A persistent VRR offers a potential autism endophenotype. Further characterization of the VRR and other primitive reflexes in ASD is needed to assess their emergenicity and possible utility in assessing early risk to ASD with and without ID. The investigation of possible neurobiological and genetic associations is warranted. Studies that include family members and younger subjects should be particularly informative.

134.60 60 Early Neurological Impairments in Children with Autism Spectrum Disorders. N. Gaddour*, A. Bedoui, N. Jabnouni, S. Missaoui and L. Gaha, *University of Monastir*

Background:

As neurodevelopmental disorders, autism spectrum disorders (ASD) are often associated to early impairments of central nervous system. Perinatal anoxia and febrile convulsions are among the most frequent ones. In Tunisia, progress in medical care for delivery and early infancy led to a dramatic decrease of childhood death, but to an increasing rate of early neurological impairments

Objectives:

to estimate the frequency of early neurological impairements in children with ASD.

Methods:

Systematic records of medical data during delivery and early childhood for all the consecutive patients with ASD at the outpatient clinic of child psychiatry in the University Hospital of Monastir, from 2003-2008(N=211). Data were collected from the Child Health Notebook systematically filled during delivery and regular check-ups.

Results: 29% of ASD children experienced perinatal anoxia and 18% febrile seizures. Early neurological impairments were not necessarily correlated to severity of autism or to comorbidy with medical conditions.

Conclusions: Through this evident association, better prevention from obstetric complications and early childhood morbidity should participate to the prevention of some forms of ASD.

134.61 61 Pharmacotherapy in Children with ASD: Baseline Findings from the New Jersey Autism Study. W. Zahorodny*, B. Peng and T. Patel, *University of Medicine and Dentistry of New Jersey*

Background: Though behavioral and educational interventions are the mainstays of treatment, children with Autism Spectrum Disorders (ASD) are also prescribed psychoactive medicines. The extent to which pharmacotherapy plays a role in the treatment of autistic children is not well understood. The few surveys of this topic have not established representative epidemiologic estimates. Objectives: This study was undertaken to estimate of the number, proportion and demographic distribution of children with ASD receiving pharmacotherapy with psychoactive drugs, in a large and diverse New Jersey population-based sample and to describe the frequency of psychoactive treatment by drug type. Methods: Data were collected as a part of the New Jersey Autism Study (NJAS), a population-based ASD surveillance investigation carried out in Essex, Union, Hudson and Ocean Counties, a diverse, populous, metropolitan region. Baseline findings represent 8-year olds (1992-born), in 2000. ASD ascertainment was by an active, retrospective, multiple-source, case-finding method, developed by the Centers for Disease Control and Prevention (CDC), based on review and analysis of information contained in health and education records. Demographic variables and case-specific data, including information on the prescription of psychoactive medicines were analyzed. The socioeconomic status (SES) of ASD cases was represented by the District Factor Group (DFG) ranking, a community-level index. Chi-square test was used to test associations. Results: 295 children with ASD were identified from a total 8-year old population of 29,748. 97 of the 295 ASD children (32.8%) were prescribed one or more psychoactive drug, at any time before or during their eighth year. Stimulants were by far the most frequently prescribed drug type, being provided to 69 children (23% of the total ASD cohort). Anti-depressants (7%), anti-psychotics (7%), α-2 adrenergic agonists (6%), sedatives (2%) and other psychoactive drugs (10%) were prescribed less frequently. Overall, the frequency of psychoactive prescription did not vary significantly by sex, race/ethnicity or SES. When analyzing the prescription of medicine by drug type, however, white children were found to be prescribed antidepressants more frequently than children of other races ($p<0.05$) and children from high SES communities were more frequently prescribed anti-depressants than children from lower and mid SES towns ($p<0.001$). Conclusions: In 2000, one third of 8-year old ASD children in our region had been treated with psychoactive medicines. The frequent prescription of stimulants to children with ASD underscores the importance of attention deficits as an associated feature of ASD. The greater frequency of anti-depressant prescription to white children and affluent children may suggest a subtle disparity in the provision of pharmacotherapy. Continued monitoring of children with ASD in the region by a population-based method may disclose trends in the

frequency and pattern of psychoactive treatments provided to children with ASD.

134.62 62 Neuro-Developmental Disabilities Screening and Assessment in Uganda. A. Kakooza-Mwesige*[1] and J. K. Grether[2], (1)*Makerere College of Health Sciences*, (2)*Sequoia Foundation*

Background: Neuro-developmental disorders, including autism, are noted to be one of the greatest threats to global public health, especially in developing countries. In low resource settings, there is a paucity of data on the number of children affected by neuro-developmental disorders and their demographic characteristics. Obtaining data on autism spectrum disorders (ASD) is especially challenging, due to numerous factors, including higher priority causes of childhood morbidity and mortality, prevailing poverty and associated health, nutrition, and social factors, and cultural beliefs and practices that impact on community recognition and integration of ASD-affected individuals. Difficulties exist in establishing ASD diagnoses based on behavioral criteria and it is not clear whether clinical presentation is similar across diverse cultural settings, presenting an inherent circularity in attempting to adapt screening and diagnostic tools. Furthermore there are few clinical practitioners trained to diagnose ASD and provide appropriate advice to caregivers. Support services for parents and other family members are minimal. Despite these numerous challenges, we are initiating an ASD screening and assessment project in the sub-Saharan country of Uganda, nested in the context of a broader neuro-developmental screening and assessment project The Uganda project will focus on autistic spectrum disorders, cerebral palsy, epilepsy, mental retardation, speech and language disorders, hearing impairment, and visual impairment among 2-9 year old children.

Objectives:

1. To develop and pilot, a screening and assessment tool for neuro-developmental disorders, including ASD, for use in Uganda.

2. To develop a plan for a comprehensive training program and other local infrastructure requirements.

3. To strengthen the research and clinical capacity of Ugandan researchers by establishing in-country and international networks.

Methods: For screening purposes, we will adapt and expand a neuro-developmental screening tool previously validated for use in low-resource settings, TQQ (Ten Questions Questionnaire), to include screening questions for ASD and speech and language disorders. These additional questions will be developed through a series of collaboration meetings with Ugandan and American clinicians. The expanded TQQ will be piloted in Uganda for use in door-to- door screening, to be followed by full clinical assessments of children who screen positive and a sample of children who screen negative to assess the sensitivity and specificity of the screening tool. Screening will be conducted in two districts in Uganda representing rural and urban communities. Culturally appropriate interventions will be provided following the clinical assessments.

Results: The focus of this presentation will be on the ASD and speech and language screening questions, how they were developed for this project, and on initial pilot testing of the questions. The clinical consensus criteria used to diagnose a child with ASD will be discussed.

Conclusions: The results of this study will provide important information on how the TQQ can be used to screen for ASD and other neuro-developmental disorders in a resource-poor African country. Data generated on the frequency and impact of these conditions will be used to advocate for appropriate sustainable services and prevention strategies.

134.63 63 Randomized Placebo-Controlled Trial of Hyperbaric Oxygenation Therapy. D. Granpeesheh[1], J. Bradstreet[2], J. Tarbox*[1], D. R. Dixon[1], S. Allen[1] and A. E. Wilke[1], (1)*Center for Autism and Related Disorders*, (2)*International Child Development Resource Center*

Background:
Autism Spectrum Disorders (ASDs) are characterized by significant challenges in socialization, communication and stereotypical behaviors. While hundreds of treatments for ASDs exist, very few have been subjected to sound scientific investigation. One popular treatment which has been the subject of little previous research is hyperbaric oxygen therapy (HBOT). While a large amount of anecdotal and uncontrolled reports suggest that HBOT is an

effective treatment, only one controlled study has been published, consisting of a multiple baseline across three children. No treatment effect was detected in that study but further replication across additional participants and within a randomized placebo-controlled design is needed.
Objectives:
The objective of the current study was to evaluate the effects of HBOT, in a preparation similar to how it is typically used in the community, on language, socialization, stereotypy, and diagnostic outcome of children with autism.
Methods:
The current study consisted of a randomized placebo-controlled trial of HBOT. "Soft-shelled" HBOT chambers were used, such as are typically used in the general community. HBOT treatment sessions involved sitting in a chamber and being exposed to 24% oxygen at 1.3 ATA for 80 1-hour treatments. A minimum of six and a maximum of 10 treatments were administered per week. Placebo consisted of sitting in an HBOT chamber with normal atmospheric oxygen concentration and pressure. Parents were not informed of which group their child was assigned to. Both direct observational measures of behavior and standardized psychological assessments were used to evaluate the effects of the treatment. Behavior data collectors and psychological assessors were blind to group assignment. All areas of participant functioning relevant to autism were measured before and after the treatment phase, including language, challenging behaviors, play, stereotypy, and socialization. The Autism Diagnostic Observation Schedule and the Social Responsiveness Scale, both diagnostic measures of autism, were also included before and after treatment. All participants were concurrently receiving applied behavior analytic (ABA) therapy but the number of ABA treatment hours received was matched between the two groups. This was done to control for the potential confounding effects of differing number of ABA treatment hours between groups because ABA is a treatment of proven effectiveness.
Results:
Statistical analyses revealed that both groups improved slightly from baseline to post-treatment but no differences in outcome were detected between HBOT and placebo groups in direct measures of behavior, the results of standardized assessments, or the results of diagnostic assessments.
Conclusions:
The results of this study suggest that HBOT is not an effective treatment for autism. This study constitutes the first randomized placebo-controlled evaluation of HBOT.

134.65 65 Three-Dimensional Photogrammetric Analysis of Soft Tissue Facial Morphology in Autism. G. Emgushova*[1], R. T. McIntosh[1], P. Gautam[1], S. J. Spence[1], A. Thurm[2], S. E. Swedo[2], S. Mitchell[1], T. C. Hart[1] and D. L. Domingo[1], (1)*NIH*, (2)*National Institute of Mental Health, National Institutes of Health*

Background: Subtle dysmorphogenesis of the craniofacial region may constitute important corroborating evidence of the neuro-developmental aspects of various disorders. The etiology of autism remains unclear, but some data suggest aberrant circuitry in the cerebral cortex and impairments in brainstem, cerebellar, thalamic and basal gangliar connections. Effects on motor neurons which innervate the facial musculature and soft tissues suggest possible consequences related to the development of facial morphological patterns. Previous studies have associated facial features with neuro-developmental disorders, but there is paucity of data on facial morphometrics in autism. Assessment of facial features also has been challenging due to the subjective nature of conventional analytical methods.

Objectives: The aim of this study is to objectively analyze the facial characteristics in autism using three-dimensional (3D) computerized surface tissue models (stereophotogrammetry) in comparing facial features of children with autistic disorder (AD) and those with typical development (TD).

Methods: Twenty-nine Caucasian AD children (21 males, 8 females, age range: 2-7 years, mean: 4.2 years) and 29 Caucasian age- and gender-matched TD children were imaged using stereophotogrammetry (3dMDface System™). Autism diagnoses were based on ADI-R, ADOS and clinical judgment. The following age groupings were formulated for both AD and TD: Group I, age 2-3 years, n=17; 12 males, 5 females; Group II, age 4-7 years, n=12; 9 males, 3 females. Computerized dense surface models (DSM) were marked with 14 homologous facial landmarks and, using Procrustean superimposition, were combined to form mean 3-D facial models. Analyses were performed using the following Morphostudio™ algorithms: (1) finite-element analysis (FEA), which compared

deviations in facial forms as a function of volume; (2) function manager analysis (FMA), which calculated numerical linear and angular parameters; and (3) principal components analysis (PCA)), which formulated graphical outputs calculated from the position of individual DSM's in the X-and-Y axis modal space.

Results: Comparisons of mean AD and TD facial models yielded no significantly measurable differences between the two groups. FEA-calculated volume and deformation factors revealed no statistically significant differences between AD and TD in both age groups ($p>0.05$). Linear dimensions (e.g., intercanthal distance, nose width, upper-, mid- and lower-facial lengths) and angular measurements (e.g., lower facial profile, maxillary complex profile) generated by FMA yielded no numerical parameters that exceeded levels of significance. PCA-generated graphical outputs (formed by enclosing ellipses around the groupings) revealed no significant differences in the geometrical dimensions outlined in the modal spaces. The near complete merging of AD and TD ellipses for both age groups demonstrated the absence of meaningful deviations between the two groups.

Conclusions: Computerized morphometrics objectively quantified the facial features in autistic children. Our analyses revealed no statistically significant deviations in any of the measurements or indices between AD and TD. As this study has been conducted in very young subjects undergoing periods of active facial growth, future analyses may pursue possible significant facial patterns that emerge in older autistic populations.

134.66 66 Facilitating Pediatrician Buy-in: a Technological Solution for Integrating An Autism Screener into the Medical Office Work Flow. R. I. Arriaga*[1], O. Ousley[2], B. Van den Bogaard[3], S. Kannan[3], G. D. Abowd[1] and J. M. Rehg[3], (1)*Georgia Institute of Technology*, (2)*Emory University*, (3)*Georgia Tech*

Background: Following the CDC report that approximately 1 in 150 children in the United States has an autism spectrum disorder (ASD), the American Academy of Pediatrics has released clinical guidelines recommending that pediatricians screen all infants for autism, at 18- and 24- months, during well baby checkups. In the managed care environment where doctors may have limited time to spend with each patients, the question then becomes how do we make it feasible for physicians to engage in the systematic use of a given autism screening instrument?

Objectives: Our goal was to design a technological solutions that would facilitate the integration of an autism screening form into the medical office's work flow and to engineer incentives that would provide value added data for the physician.

Methods: We conducted a case study on a parent who had well baby checkup experience for two children from 2005-2008. The well-baby visit protocols were analyzed for two medical offices in two states. The routines were found to be very similar. First, a staff member would measure the child's height, weight and head circumference. Then the physician would discuss the measurements with the parent, making reference to how the child compared to the norm. In one case, the parent was given a print out of the child's longitudinal data to keep for her records. The case study also revealed that because the family relocated to another state the older child saw different pediatricians during the second year of life.

Results: Our case study suggests that in order to increase physician buy-in to the practice of screening for autism at 18- and 24-months the medical staff must administer and process all logistical issues related to the instrument and physicians should be provided with data concerning normed values. We also found that continuity of care cannot be assumed and that physicians need to have access to longitudinal data. Thus we created a software program that accounts for these factors in two steps: scanning a demographic sheet and the autism screener. The software generates a personal identification code using the 4 questions on the demographic sheet. When the screener is scanned the program automatically tags it with the id, scores the screener and stores the results. Our program then generates data concerning the child's performance compared to the normed values and if applicable, data from the child's 18-month results. The staff can then give these to the physician and the parent.

Conclusions: To date researchers that study ASD have devised many screening and diagnostic tools. However, there has been little research into how these tools can be integrated into the work flow of the medical office to ensure physician buy-in. The next step for our study is to deploy our

program in local medical offices. The technological solution we propose has the potential to penetrate the work flow of pediatrician's offices because it follows standard protocol that are the mainstay of well baby visits and provides comparison to normed values as well as longitudinal data across different medical offices.

134.67 67 Association of Insurance Type and Cost, Use, Accessibility, and Outcomes of Services for Children with ASD. A. M. Young*[1], L. A. Ruble[1] and J. H. McGrew[2], (1)*University of Kentucky*, (2)*Indiana University - Purdue University Indianapolis*

Background:

Therapeutic care for a child with autism is often extremely complex, entailing a high rate of service utilization and a multifaceted approach to treatment. In turn, parents of children with autism often report problems with accessibility, coordination, and family-centeredness of care, as well as problems with adequacy of insurance coverage. Despite the apparent interrelatedness of these issues, research into the association between insurance coverage and indirect costs, outcomes, and accessibility of services for children with autism is lacking.

Objectives:

The purpose of this study is to compare private and public insurance coverage for children with autism in terms of several interdependent variables -- (a) out-of-pocket expenditures, (b) variety of services used, (c) access to services, (d) child and family outcomes of services, and (e) satisfaction with the payer of services. Due to the exploratory nature of this study, no directional hypotheses were proposed.

Methods:

This study is a secondary analysis of a larger examination of parent and caregiver experiences with the service system in one state (further details on methods are reported in Ruble and McGrew (2007)). The 43-item survey regarding services received in the prior 6 months was distributed to parents/caregivers of children with ASD through direct dissemination at parent support groups, at a special educator meeting, via mail using state databases of community mental health centers, via the internet for autism listservs, and via a web-based version of the survey. Items from the survey were used to construct the five variables to be evaluated against type of insurance: (a) out-of-pocket expenditures, (b) variety of services used, (c) access to services, (d) child and family outcomes of services, and (e) satisfaction with the payer of services. The questionnaire targeted nine specific services - inpatient care, medication management, counseling or training, individual therapy, in-home behavior therapy, speech and language therapy, occupational therapy, case management, respite care, and contained one set of questions for "other service."

Results:

Of all respondents (n=107), 70.8% were privately insured while 19.5% were publicly insured (9.7% did not report insurance type). No statistically significant differences in out-of-pocket expense, variety of services used, child and family outcomes, or satisfaction with payer were found among privately and publicly insured children. However, a Mann-Whitney U test did reveal that publicly insured children used significantly more medications than did privately insured children (p=0.028). Also, an independent-samples t-test revealed that mean ratings on the *access to services* subscale (Cronbach's alpha = 0.703) were significantly higher among privately insured children than publicly insured children (p=.036).

Conclusions:

Among parents of children with autism residing in the state of, private and public insurance coverage is similar in terms of out-of-pocket expense, variety of services used, child and family outcomes of services, and satisfaction with payer. However, parents of privately insured children with autism may have better access to services than do parents of publicly insured children.

134.68 68 Children with Special Health Care Needs: Evaluating Care Coordination Services for Children Diagnosed with An Autism Spectrum Disorder. C. Burns*, M. Orlando, S. Sulkes, D. W. Mruzek, K. O'Mara, E. Hebert, S. Nichols, L. N. Barzotto, M. Ryan, D. Vogler-Elias, J. Roesser and P. Gemmell, *University of Rochester Medical Center*

Background: Due to technological advancements and changes in society's attitude, children with special health care needs, in particular those with Autism Spectrum Disorder (ASD), have more treatment options available to them. These children are more likely to reside in private homes, attend public schools, and to utilize a

variety of different medical and educational services. As a result, the medical care of these children has become more complicated and the shift to managed care health plans has resulted in administrative issues that must be addressed in order to receive services. The lack of a single entry point linking systems of health care, social services, education, public health services, and home services makes coordination of care difficult (AAP, 1999). Emerging electronic information sharing systems (EIS) hold particular promise for improving the coordination of care of children with ASD.

Objectives: The purposes of this investigation are to evaluate professional perception of effort in coordinating services for children who have a diagnosis of an ASD, to evaluate professionals' satisfaction of care coordination services they provide to families of children with an autism diagnosis and to determine the usage of electronic medical records or electronic information systems for providing care coordination services. The data obtained in the study will be used to identify factors that may promote successful care coordination and identify areas where additional supports would benefit children with a diagnosis of an ASD, their families, and professionals.

Methods: Eight hundred participants from four groups: a) the Autism Treatment Network; b) the Autism Special Interest Group of the Association for University Centers on Disabilities; c) the Leadership Education in Neurodevelopmental and related Disabilities network; d) the University Center for Excellence in Developmental Disabilities network received an on-line survey examining: Demographics, Background, Current Disclosure Practices, Barriers to Effective Disclosure, Recommendations, Electronic Medical Record Use, Care Coordination with EMR/EIS, Care Coordination Practices, and Transitions. The survey was designed after thorough literature review and qualitative data gathered through focus groups and then stringently tested and reviewed for its face and content validity by 10 subject matter experts in the field of ASD. Participants' responses to the survey were analyzed through quantitative statistical methods (i.e., descriptive statistics, including percent, mean response levels, range of responses), as well as qualitative methods (i.e., review and analyses of written responses).

Results: Preliminary data analysis revealed that considerable variability in care coordination practices continues to exist and significant barriers in communication among providers in health care, financial and school settings and in accessing information about community resources prevail. Satisfaction with care coordination for children with ASD was associated with the scope and extent of electronic information system use. EMR use facilitated decision-making, receiving immediate responses to problems, and assistance with treatment plan implementation and transition planning.

Conclusions: Use of EIS and EMR must be increased to assure family-centered care and improved care coordination enhancing health and functional outcomes of children with ASD.

134.69 69 Trends in Diagnostic Testing Practices for ASD in a Population-Based Sample from Philadelphia County. E. Giarelli[1], L. C. Lee[2], J. Pinto-Martin*[1], S. E. Levy[3] and R. Meade[1], (1)*University of Pennsylvania*, (2)*Johns Hopkins Univ. School of Public Health*, (3)*Children's Hospital of Philadelphia*

Background: Trends in the use of diagnostic evaluation tools are not well described, especially in high density urban areas where minority populations are typically large. Data collected for the Pennsylvania Autism and Developmental Disabilities Surveillance Program (PADDSP) of the ADDM Network will be analyzed to characterize the use of diagnostic and/or screening tests among cases of ASD in Philadelphia County over two study years, 2002 and 2006. In 2002 a total of 111 eight-year-old children were identified to meet the DSM-IV-TR (APA, 2000) criteria for the ASDs. The calculated prevalence was 5.3 per 1,000 8 year olds. The prevalence of ASD among 8-year olds in Philadelphia County in 2006 will be reported in February 2009.
Objectives: The purpose of the presentation is to describe, (1) the proportion of cases who received an ASD diagnostic evaluation stratified by sex and race/ethnicity for each surveillance year (2002 and 2006), (2) the distribution of ASD test type by sex and race for each surveillance year (2002 and 2006), (3) changes over time in the use of diagnostic test instruments among cases who had a previous ASD diagnostic evaluation; (4) changes over time in the distribution of provider specialty administering ASD diagnostic evaluation.
Methods: Data will include the reports of the specific ASD diagnostic tests used for children in

Philadelphia County as recorded in the PADDSP database. These include: the Autism Behavior Checklist (ABC), the Autism Diagnostic Interview-Revised (ADI-R), the Autism Diagnostic Observation Schedule (ADOS), the Childhood Autism Rating Scale (CARS), the Gilliam Autism Rating Scale (GARS), the Gilliam Asperger's Disorder Scale (GADS), or other ASD Test. We will use data from the PADDSP site, only, for study years 2002 and 2006. Data will be analyzed descriptively using frequencies, proportions, etc.
Results: (Preliminary, 2002 SY ONLY)
Of 111 cases, 28 (25%) mentioned an ASD test in the child's records. The most commonly used ASD evaluation was the CARS followed by GARS and Other. ADOS and ADI-R were used rarely (4% of cases).There is no difference in the kind of evaluations used for non-white and whites or males and females. White males and non-white females were evaluated at an average age of 59 mo. AA males were 1st evaluated at the oldest age (76mo). Evaluations were conducted by psychologists (49%), developmental pediatricians (29%), other or unknown (16%), and an educator (6%).A child's first ASD evaluation was most often performed by a psychologist (51%) at an average age of 69 mo. 28% of first evaluations were conducted by a developmental pediatrician at an average age of 74 mo.

Conclusions: Pending analysis of data from the 2006 Study Year. We will compare our findings to the report of the use of tests in four other Surveillance states in which there was a steady increase in the proportion of children evaluated using one or more ASD diagnostic tests.

134.70 70 Level 2 Pervasive Developmental Disorder Rating Scales.

M. Norris* and L. Lecavalier, *Ohio State University*

Background: Rating scales are an attractive means by which to screen for Pervasive Developmental Disorders (PDDs) due to their ease of administration and low cost. They are also used to determine eligibility for services or research studies and to measure change. Many rating scales have been developed for screening purposes, making it difficult for professionals to select the most appropriate and effective instrument for their target population. Although reliable diagnosis of PDDs can be made as young as 20-24 months (e.g., Cox et al., 1999; Stone et al., 1999), several studies have reported diagnoses to be delayed several years and to occur in older children (e.g., Wiggins et al., 2006; Sivberg, 2003).

Objectives: To review the peer-reviewed literature on the diagnostic validity of level 2, caregiver-completed rating scales for the screening of PDDs in school-aged children (ages 5-12 years).

Methods: PsycInfo database was searched with combinations of the terms "PDD," "autism," "Asperger Disorder," "PDD-NOS," "rating scale," "screen," and "screening instrument." Inclusion criteria required that scales: (a) be developed post-ICD-10; (b) be PDD-specific; (c) have published diagnostic validity evidence in peer-reviewed journals; (d) be level 2 instruments; and (e) focus on school-aged children. Diagnostic validity was evaluated based on sensitivity and specificity values (values >.70 and .80, respectively, were considered good), positive and negative predictive power, and AUC (higher values were considered desirable). Special attention was paid to the choice of comparison groups for diagnostic validity.

Results: Five scales met inclusion criteria: the Social Communication Questionnaire (SCQ), Gilliam Autism Rating Scale- Second Edition (GARS-2)/Gilliam Autism Rating Scale (GARS), Social Responsiveness Scale (SRS), Autism Spectrum Screening Questionnaire (ASSQ), and Asperger Syndrome Diagnostic Scale (ASDS). Review of published studies indicated that the SCQ has received the most examination, with more studies of diagnostic validity than the other four scales combined (n=11). Available evidence for the remaining four scales was limited. Contrast groups varied significantly across studies and impacted results significantly. Overall, studies on the diagnostic validity of the SCQ indicated that it performs well at different cut-offs for different groups, although performance was poorest in younger individuals. No independent studies of the GARS-2 are available. Three of the four studies examining diagnostic validity of its predecessor, the GARS, indicated poor sensitivity. The SRS has limited evidence of diagnostic validity but appears promising. Limited support is available for the ASSQ, though it has demonstrated adequate sensitivity and high specificity. Only one independent study has examined the ASDS and it suggested poor diagnostic validity.

Conclusions: Results of this review indicate level 2 PDD caregiver-completed rating scales are in need of much more scientific scrutiny. The SCQ is a

strong choice for screening, while the SRS and ASSQ show promise. The GARS and ASDS should be avoided in diagnostic contexts.

134.71 71 A Training Model for the Diagnosis of Autism in Community Pediatric Practice. Z. Warren*[1], W. Stone[1] and Q. Humberd[2], (1)*Vanderbilt University*, (2)*Blanchfield Army Community Hospital*

Background:

Early screening and diagnosis of autism spectrum disorders (ASD) currently represents a critical public health and clinical practice issue. Historically, waits for diagnostic services are quite lengthy and hinder the start of early intervention services thought to be crucial for optimizing functional developmental outcomes for children and their families.

Objectives:

In this study we developed and evaluated a training program designed to help pediatricians identify and diagnose young children with ASD in the context of traditional community practice settings within a very time-limited framework (1 hour).

Methods:

Five community pediatricians participated in an intensive training (i.e., use of MCHAT, Screening Tool for Autism in Two-year-olds (STAT), and focal diagnostic interviewing), conducted specialized 1-hour ASD diagnostic evaluations within their own practices, and then referred a consecutive series of children to a traditional medical center diagnostic clinic for an independent assessment of ASD.

Results:

Of the five community physicians attending the START-ED training, four referred patients for subsequent independent evaluation. 21 or 25 referrals completed the independent evaluation process (child age M = 30.48, SD = 3.74). Of the four families who declined invitation to participate in the evaluation, only one had received an ASD-risk classification from their referring pediatrician. Of children seen for independent evaluation, 19 (90%) received diagnoses of ASD-risk from their pediatrician. An ASD diagnosis was confirmed based on independent evaluation in 14 out of these 19 cases (74%). Of the 2 children (10%) referred without an ASD-risk classification, one child received a diagnosis of ASD subsequent to independent evaluation and one did not (50% agreement). Overall independent diagnostic evaluation was in agreement with initial pediatrician classification in 15 out of 21 cases (71%). Agreement varied greatly between the four referring pediatricians: 1/1 = 100%; 6/7 = 86%; 4/6 = 67%; 4/7 = 57%.

In all cases (n=6) where there were diagnostic disagreement clinically significant developmental concerns were confirmed during the independent evaluation (i.e., global developmental delays or speech/language delays). Clinical diagnostic certainty ratings from the independent evaluation process were significantly lower for children not receiving an ASD diagnosis (ASD mean = 4.27; Non-ASD mean = 2.41; $t = 3.72$, $p < .05$).

Conclusions:

The development of training methods for the classification of ASD within traditional community based pediatric practice holds promise. Specifically, introduction of basic interactive screening tools into a pediatric consultative model may be able to successfully classify young children in a timely fashion to appropriate categories of risk. Such models must take into account the reality that significant revision and condensation of gold-standard assessment methodologies will undoubtedly contribute to more errors in definitive classification. However, if we are able to train community providers to identify risk and initiate intervention services based on such assessed risk status, long waits for more definitive diagnostic assessment services will not hold deleterious effects for the child, nor will clinicians be asked to provide definitive diagnoses within a timeframe that it is unrealistic to expect clear-cut meaningful classifications.

134.72 72 Changes in Diagnostic Testing Practices for the Autism Spectrum Disorders (ASDs) in Four US Populations. C. E. Rice*[1], J. Baio[1], M. J. Morrier[2], L. D. Wiggins[3], N. Hobson[4], L. C. Lee[5], J. S. Nicholas[6], L. A. Carpenter[6] and S. Pettygrove[7], (1)*National Center on Birth Defects and Developmental Disabilities*, (2)*Emory University*, (3)*Centers for Disease Control and Prevention*, (4)*Research Triangle Institute*, (5)*Johns Hopkins Univ. School of Public Health*, (6)*Medical University of South Carolina*, (7)*University of Arizona*

Background: Autism Spectrum Disorders (ASDs) are more commonly diagnosed today than they were in the past. Practice parameters recommend

the use of standardized tools when considering an ASD diagnosis, although little research has been done to characterize the use of these tools in large populations.

Objectives: To characterize changes in the use of ASD diagnostic tools.

Methods: The Autism and Developmental Disabilities Monitoring (ADDM) Network has been formed to track prevalence and describe the population characteristics of children with ASDs in multiple areas of the United States. Use of ASD diagnostic tests were analyzed from the ADDM Network sites in four US populations (areas of AZ, GA, MD, and SC) over three time periods (2000, 2002, and 2004 surveillance years).

Results: A total of 1,985 eight-year-old children met *DSM-IV-TR* criteria for an ASD through systematic review of evaluation records from multiple sources. Of these children, 64.7% were evaluated by a professional using an ASD test. There was a steady increase in the proportion of children evaluated using an ASD test: 56.4% in 2000, 64.7% in 2002, and 71.3% in 2004 (χ^2=32.3, p<.001). ASD test use increased significantly for both boys (p<.001) and girls (p<.001). Test use increased more sharply for girls, so while boys were more likely than girls to have had an ASD test in 2000 (p<.001), but by 2004 the proportions were similar (p=.299). There was a significant increase in the use of ASD tests for both White (p=.001) and Black children (p<.001), but not for Hispanic children (p=.112). ASD tests were used at similar proportions for White and Black children in the 2000 cohort (p=.978), but test use rose more sharply for Black children (from 58.3% to 73.3% to 79.9%) than for White children (from 58.5% to 60.3% to 70.4%). Consequently, Black children were more likely to be evaluated using an ASD test in both 2002 (p=.002) and 2004 (p=.011). Of the ASD tests given, the Childhood Autism Rating Scale was by far the most commonly used (62.5%), followed by the Gilliam Autism Rating Scale (GARS; 14.9%), Autism behavior Checklist (5.5%), Autism Diagnostic Observation Schedule (ADOS; 5.0%), Gilliam Asperger's Disorder Scale (3.4%), Autism Diagnostic Interview (ADI; 2.7%), and another ASD test (6.0%). Increased use of the ADOS, ADI-R, and GARS relative to other tests was evident. ASD tests were more often administered in school settings (64.6%) than health settings (33.6%), and were utilized most commonly by Ed.S. psychologists (30.9%) followed by Ph.D. psychologists (19.8%), developmental pediatricians (8.0%), Masters-level psychologists (8.0%), and Ed.D. psychologists (6.1%). Neurologists and psychiatrists (both 0.4%) rarely reported the use of an ASD test. The mean age of first ASD test reported was 64 months overall, with no significant change over time (p=.483).

Conclusions: Given that ASDs are behaviorally-defined disorders, the use of standardized tools is recommended for the diagnosis of these conditions. Although improvements were made over a four year period in the use of standardized tools, the use of "gold-standard" tools (the ADOS and ADI) remained low in these community settings.

134.73 73 The Each Child Study: Early Autism Screening in a Pediatric Practice. J. Miller*, T. P. Gabrielsen, M. Villalobos, B. Segura and N. Wahmhoff, *University of Utah*

Background: Systematic screening for autism in toddlers can lead to earlier identification and intervention. It may also improve our understanding of the epidemiology and clinical course of ASDs. However, the feasibility and utility of comprehensive screening is not yet established.

Objectives: We collaborated with a community-based pediatric practice to conduct autism screening for toddlers seen during a six-month period. Objectives included outlining methods for conducting screening in a pediatric practice, estimating the rate of significant ASD-related concerns in toddlers, and comparing screening results to parent and pediatrician concern levels.

Methods: A large pediatric clinic with a diverse ethnic and socioeconomic patient base was approached for participation. Researchers met with physicians and staff to determine an optimal method for incorporating screening questionnaires into their care service. Screening took place over a six-month period, and included all children born in 2006 who were seen for sick or well-child visits. Office staff distributed and collected screening questionnaires while parents waited for appointments. Parents and providers were also asked to indicate their current level of concern about the child's development (before knowing screening results). Research staff obtained all necessary permissions to obtain the clinic's daily schedule in order to determine how many eligible children were screened or missed. Office staff received daily contact from researchers to maintain compliance, and were motivated with

feedback about individual rates of completed screenings. Both the Modified Checklist for Autism in Toddlers (M-CHAT; Robins et al., 2001) and Communication and Symbolic Behavior Scales Developmental Profiles Infant Toddler Checklist (CSBS-ITC; Wetherby & Prizant, 2002) were administered. Researchers scored all questionnaires, and positive screens were followed up with phone interviews and in-person evaluations (ADOS; Lord et al., 2000 and Mullen Scales; Mullen, 1995) where appropriate. All forms were also available in Spanish, and a Spanish-speaker administered phone follow-up and in-person evaluations when appropriate.

Results: The clinic screened 81% of eligible children. The group closely reflected ethnic and socioeconomic diversity statewide. Of the 817 children screened, 24% failed either the M-CHAT or CSBS-ITC or both. Of those, 42% were eliminated as false positives after the phone interview; 38% could not be reached. Of the remaining 20% (n=44), 57% (n=25) came for an in-person evaluation. Two more were evaluated based solely on parent or pediatrician concern. Thirteen children were identified as showing significant early signs of autism; 8 were already of concern to parents or pediatrician, including 3 who had already been diagnosed. Fourteen children showed speech or other developmental delays (6 were already of concern to parents or pediatrician). One appeared to be developing typically, and was not of concern to the parents or pediatrician. Of the 27 children seen in person, 11 had been referred to early intervention services.

Conclusions: Systematic screening identified possible autism in children that were not of current concern to parents or pediatricians. Our high rate of screening questionnaire compliance was likely due to removing the burden of scoring and interpretation from the pediatricians, as well as our frequent feedback to staff and physicians.

134.74 74 Using the Spanish Version of MCHAT in a Population Based Autism Screening Program. R. Canal-Bedia*[1], M. V. Martín Cilleros[1], Z. Guisuraga Fernández[1], L. Herraez[1], M. Herraez[1], A. Martinez[1], P. García-Primo[2], M. J. Ferrari[2], J. Santos Borbujo[3] and M. Posada de la Paz[2], (1)*Universidad de Salamanca*, (2)*Carlos III Health Institute. Rare Diseases Research Institute*., (3)*UNIVERSIDAD DE SALAMANCA*

Background:

Early detection of autism has clear positive effects on prognosis, but a significant delay in obtaining an ASD diagnosis is found in Spain. For these reasons the University of Salamanca and the Institute of Health Carlos III carried out the Spanish validation of MCHAT and developed a population based screening for ASD in the public Health.

Objectives:

1. To check out if the population screening for ASD can work in the public Health System.
2. To instruct paediatricians of Primary Care Services, and to improve their awareness about ASD.
3. To improve coordination among health, social, and educational services.
4. To reduce the delay in the detection, diagnosis procedure, and treatment for children with ASD, and to reduce the family stress.
5. To estimate the incidence of ASD in the studied population

Methods:

Period: From September 2005 to December 2008
Place: Provinces of Salamanca and Zamora (Spain)
Population: 12.952 children in Salamanca and 5.761 children in Zamora that come up one of the to two compulsory paediatricians visits: vaccination at 18months and general follow-up at 24months.
Procedure:
1. Handing over of the MCHAT questionnaire and the informed consent to the families when they attend to the paediatrician with a child 18 months and 24 months old.
2. Telephone interview in positive cases following the flow-chart format for exploration of each failed item (Robins, 2001).
3. Referral to the Childhood Unit of the University of Salamanca for a specialised evaluation of the confirmed positives cases (ADOS-G, ADI-R, MERRIL PALMER –R, VINELAND).
4. Search of "false negatives" through a randomized sampling selection of negative cases. A telephone interview exploring each DSM-IV-TR criteria for Autistic Disorder was carried out for

each selected child.
5. Referral to the public Early Intervention Program of those cases finally diagnosed with ASD, SLI, developmental delays, etc.

Results:

Global response rate (total of children): 5726/18713=30.59%
Total questionnaires received: 5726 (1827 at 18 months visit in Salamanca and 1281 at 18 months visit in Zamora; and 1504 at 24 months visit in Salamanca and 1114 at 24 months visit in Zamora).
Response rate in Salamanca = 3331/12952 (25.71%)
Response rate in Zamora = 2395/5761 (41.57%)
Positive cases in the questionnaire that follows to the second step of the telephone interview=794
Positive cases confirmed after telephone interview =35
Evaluated cases=35
1. Salamanca cases: ASD=5; SLI=3; Developmental delay=11; False positive=5.
2. Zamora cases: ASD=4; SLI=2; Global developmental delay=5)

Prevalence: 1.6 per 1000

Conclusions:

The population screening program for ASD, using the Spanish version of MCHAT, showed that services coordination is possible. Also it is proved that a reduction of diagnosis delay in the public health system is possible. The study gives support that paediatricians can be involved in a detection program if they have available information and reliable resources. Nevertheless, we must to have into account the limits of our results, due to the low participation rate, and the high number of positive cases in the questionnaire, prior to the phone interview. These aspects suggest that a reform in the screening program could be necessary.

134.75 75 Clinical Practices Regarding Autism Spectrum Disorders among General Practitioners in Karachi, Pakistan and How They Compared to Practices in the United States. K. Ibrahim*[1] and M. H. Rahbar[2], (1)*Michigan State University*, (2)*University of Texas Medical School at Houston*

Background:

The prevalence of Autism Spectrum Disorders (ASD) appears to be on the rise in developed countries, and has become a serious public health concern. In most developing countries, however, the nature and prevalence of factors associated with ASDs are unknown. As the first step in conducting population based epidemiological studies in Pakistan, we conducted a survey to assess knowledge, attitudes and practices of the General Practitioners (GPs) in Karachi, the largest city in Pakistan. It is important to better understand how the medical community of Pakistan conceptualizes this developmental disorder.
Karachi provided an ideal location for an exploratory epidemiological study in Pakistan. The study location provided diversity not only in culture but also in living situations. Pakistani's migrate to Karachi from all over the Country; similarly physicians from very different backgrounds practice in this metropolitan city.
Objectives:

1. To assess clinical practices of general practitioners as it pertains to ASD in Karachi, Pakistan.
2. To compare behavioral identifiers used to diagnose autism in Pakistan and how they compare with first line diagnostic surveys used in the United States (MCHAT and CARS).
Methods:
In a study period lasting from June 2007 through August of 2007, a sample of 346 physicians were systematically selected from a database of general practitioners. We implemented a survey to better understand their knowledge, attitudes and practices as it pertained to treating patients with autism spectrum disorders.
The survey instrument compromised of three major parts:
1. Demographics: Included demographic information such as their age, sex, medical background, patient load, and area of interest in the field of medicine.
2. Knowledge and Exposure: Exposure to the term "autism" and source of exposure. Whether they had a working knowledge of autism for diagnosis.
3. Attitudes and Practices: Questions regarding their attitudes towards ASD and their diagnostic criteria. Finally, from a list of behavioral symptoms which behavioral observations are necessary, not necessary but helpful, or not

necessary in diagnosing ASD.
Results:

Among the physicians interviewed only 42 % (n=146) had heard of the term "autism". Furthermore only 17% (n =60) of the total sample size indicated they had a working knowledge to diagnose ASD. Only subjects from this latter sample were asked questions regarding their practices.
Out of the physicians who made it to the practices section of the survey the vast majority correctly identified impaired social interaction and impaired communication as potential identifiers for ASD (92%,83%). On the other hand, 23% said "hearing voices" was "necessary" in making a diagnosis for ASD and 25% said it was "helpful but not necessary" for diagnosis. Similarly, 20% of this sample indicated that hallucinations were a "necessary" behavioral characteristic for diagnosing ASD.
Conclusions:

This investigation further uncovers the autism diagnosis and referral system in the cultural context of Karachi, Pakistan. It is most important to understand these criteria in order to effectively focus our attention in medical education and seminars for currently practicing physicians.

134.76 76 Evaluation of a Population Screening Program Based on Paediatrician and Families Degree of Satisfaction. L. Boada*, P. García-Primo, E. García-Andrés, E. Touriño, C. Martín-Arribas and M. Posada de la Paz, *Carlos III Health Institute. Rare Diseases Research Institute.*

Background:

Previous studies carried out by the Institute of Health CarlosIII of Spain showed a significant delay in obtaining an definitive ASD diagnosis however it was proven that a Population Autism Screening Program into the Public Health System using the *MCHAT* can reduce significantly the time needed to obtain it. One of aspects that plays an important role in decision-making for the Health Policies is the satisfaction of the state holders with this kind of programs and this was the main reason to carried out this work.

Objectives: To evaluate the grade of acceptability and satisfaction of the AutismScreeningProgram by families and paediatricians as the main state holders. To evaluate the strengths and weaknesses of the AutismScreeningProgram. To improve its future implementation in our country.

Methods:

Population target: 75 medical professionals (30 paediatricians and 45 nurses) and 818 families (a randomized sampling selection from 2908)
Procedure: Data is collected through two different questionnaires designed in based on the following variables:
1. **Paediatrician/Nurse Variables**: Research team general strategy, information given in workshops about program structure and procedure, importance of periodical reports of results, adequacy of the informed consent and the M-CHAT themselves, judgment on parents satisfaction, consequent improvement of their knowledge and surveillance of sociocommunicative early development, progress on the coordination with Early Intervention social and educational services. Also it was explored the extra time spent per child to screen ASD and their opinion about their feasibility for a future compulsory implementation of the program. 2. **Family Variables :** Paediatricians explanations, Informed consent and MCHAT questionnaire, improvement of awareness of early sociocommunicative development in their children, letter they had received regarding their child results, telephone interview in positive cases, professionals involved in the assessment and diagnosis, diagnosis report , documents of public Early Intervention Services, their access and availability, agreement with the future compulsory instauration of the program, general satisfaction with the program and with the research team.

Answers stand on Likert form where 0 is the lowest score and 4 the highest.
Questionnaires were sent and received by mail Questionnaires were sent back anonymously. The statistical analysis was carried out by STATA.10 (means and CI 95%)

Results:

Paediatrician/Nurses participation rate: 34/75 (45.33%)
Families participation rate: 200/818 (24.44%)
Most of the questions received the highest scores: 3 and 4. The aspects that were most positively evaluated by paediatricians/nurses were their impression about parents opinion about the screening program (mean=3.70[3.51-3.90]), their judgment about its future implementation

(mean=3.54[3.34-3.75]) and the research team strategy (mean=3.45[3.15-3.74]). The lowest scores were the improvement of coordination with Early Intervention Services (mean=2.87[2.5-3.23]), and the support received by NHS Managers of (mean=2.90[2.54-3.26]). Mean extra time per child 8.72min. Families: highest score was their will on future implementation of the program (mean=3.92[3.82-4.0]) and the lowest score the facilitation to access to Early Intervention programs (mean=2.22[0.84-3.29]).

Conclusions: Main state holders of the program are highly satisfied with the AutismScreening Program. This result should be had into account by Health Policy makers for future strategies on ASD early detection.

134.78 78 A Model for Expanding Community-Based Autism Assessment Services. K. Dillon, U. M. Cellupica* and G. Friedman, *Children's Treatment Network of Simcoe York*

Background: In Canada, a scarcity of developmental pediatricians and limited funding for multidisciplinary assessments has resulted in long delays for these assessments. In the province of Ontario, communities such as York Region have long suffered from a lack of resources to assess preschool children suspected of having an Autism Spectrum Disorder. As a result, many families rely on assessments that are variable in terms of adherence to best practices. The Canadian Best Practice Guidelines (Miriam Foundation, 2008) recommend that diagnostic assessments be conducted by an interdisciplinary team when possible. Further, the Guidelines suggest that the assessment include a full medical examination, administration of the ADOS and reference to DSM IV criteria. In many underserviced communities, children have been assessed by a variety of professionals using suboptimal or non-standardized assessment tools. These diagnostic limitations leave families faced with the possibility of an inaccurate diagnosis or a delay in diagnosis and treatment until an interdisciplinary assessment can be carried out.
Objectives: To demonstrate that an interdisciplinary model involving Speech-Language Pathologists and General Pediatricians can provide high quality preschool autism assessments thereby reducing wait times for assessment. Methods: The Children's Treatment Network of York and Simcoe has recently developed an innovative, collaborative model for assessment of children suspected of having ASD. Select Speech-Language Pathologists have been trained to reliably administer the ADOS to preschool children. General Pediatricians are able to incorporate information obtained from community partners, the results of the ADOS assessments, and their own clinical opinion when making a diagnosis of ASD. In ambiguous or complex cases, children can receive further assessment by a developmental pediatrician and/or other disciplines. Throughout the process, a Developmental Pediatrician is available to mentor and assist various team members. Children in York can now receive a diagnosis based on a standardized observational assessment with contributions from several members of the interdisciplinary team.

Results: Between September 1, 2007 and August 30, 2008, 54 children were assessed through the expanded service. Of those, 83% received a diagnosis of ASD (n=45). These children were an average of 38 months of age at the time of assessment (range: 23 months - 58 months). The average wait time for the assessment was 5 months. Previous to this expansion, children were waiting approximately 12 months for assessments.

Conclusions: Interdisciplinary teams utilizing ADOS-trained Speech-Language Pathologists and General Pediatricians can expand existing ASD assessment services and reduce wait times and average age of diagnosis for families. These teams need to be closely supported by Developmental Pediatricians and other professionals, such as Occupational Therapists and Social Workers. We have shown that the use of General Pediatricians integrated into an interdisciplinary model, reduced the waiting for assessment by 60% This novel approach adheres to best practice guidelines and can be implemented in other communities where access to developmental assessment services is limited.

134.79 79 Correlates of Specialized Public School Attendance among Children with Autism Spectrum Disorders. A. M. Daniels*[1], C. Anderson[2], K. Law[2] and P. Law[2], (1)*Johns Hopkins Bloomberg School of Public Health*, (2)*Kennedy Krieger Institute*

Background:

According to the Individuals with Disabilities Education Act (IDEA), children with disabilities are entitled to education in the least restrictive environment, and placement outside the regular classroom or school environment should occur only when the nature of the child's disability exceeds a

school's capacity to provide appropriate education. In consideration of the growing number of children being diagnosed with autism spectrum disorders (ASD), there is a need to better understand services provided by the public school system to these children and the extent to which children with ASD in specialized schools differ from those educated in more inclusive settings.

Objectives:

The objective of this study was to assess correlates of specialized public school attendance among children with ASD.

Methods:

Data from 3,746 school-aged children with ASD were collected from parents who completed a web-based questionnaire about their child as participants of the Interactive Autism Network (IAN) Research study. Parents were asked to report the type of school their child attended; specialized public school was defined as a school for children with special needs. Means and proportions were calculated for demographic and clinical characteristics as a function of whether a child was attending specialized public school. Group differences were tested to identify covariates significant at the $p<.05$ level that would then be included in an adjusted analysis. Multivariate logistic regression was used to estimate the independent association of these covariates and the type of school attended. Analyses were performed with Stata statistical software, Version 9.2.

Results:

Fifteen percent of the sample reported attending specialized public schools (*n*=520). In the multivariate model, younger age and having a mother with a graduate degree were associated with decreased odds of attending specialized school. Children with Aperger's (OR=0.30, 95% C.I.:0.21-0.42) or PDD-NOS diagnoses (OR=0.50, 95% C.I.:0.37-0.66) were also significantly less likely to attend specialized schools as compared to children with autistic disorder. A loss of skills was associated with an increased odds of attending a specialized school (OR=1.30, 95% C.I.:1.05-1.60) as were epilepsy and motor delay diagnoses (OR=1.66, 95% C.I.:1.20-2.29 and OR=1.31, 95% C.I.:1.06-1.61, respectively). While significant at the univariate level, neither mental retardation nor any mental health diagnosis remained significantly associated with public school type in the adjusted model.

Conclusions:

At the time of the study, fifteen percent of the sample was attending specialized public schools. Not unexpectedly, these children were significantly more impaired than their regular public school peers. Interestingly, a diagnosis of mental retardation or any mental health condition was not associated with school placement. Limitations of this study include our inability to assess the duration of attendance in specialized public schools and whether these children had previously been educated in the general school or classroom environment. Furthermore, there are likely variations in specialized school attendance by state and school district levels, which were not assessed in this study. Nonetheless, characterizing children with ASD who are educated in specialized schools has important implications for the public education system.

134.80 80 Mercury and Autism: What Do We Know? What Don't We Know?. I. Hertz-Picciotto*[1] and I. N. Pessah[2], (1)*University of California at Davis*, (2)*M.I.N.D. Institute, University of California at Davis, CCEH*

Background: The role of mercury and specifically, thimerosal-containing vaccines, in autism has received considerable attention. A few large studies have addressed this concern, using databases from health practices, health maintenance organizations, and the CDC's Vaccine Safety Datalink.

Objectives: To evaluate the strength of the evidence regarding a role for thimerosal-containing vaccines in the risk for autism. To determine what hypotheses have been addressed in those studies.

Methods: Searches were conducted using PubMed, Medline, and citations listed in previously identified original and review articles. Reports

with scientifically valid data, a minimum of 25 autism cases and a primary analysis focused on thimerosal-containing vaccines were included in the review. A total of six studies met these criteria. These studies were then evaluated for design characteristics (ecological vs. individual), presence of dose information, and the nature of the hypothesis that was tested. Potential biases in selection and uncontrolled confounding were also assessed.

Results: Two were of an ecological design (Madsen et al 2005, Schecter & Grether 2007) and four used individual-level data on vaccines administered. These four had number of vaccines administered to each child and conducted an analysis by dose or a surrogate for dose.. Doses were lower in studies conducted outside the US. In studies from Denmark (Madsen et al 2003, Hviid et al 2003), the sources of cases in the post-thimerosal period included outpatients whereas only inpatients were included in the thimerosal-exposed period, suggesting lack of comparability in case ascertainment for the two exposure periods. Several UK-based studies (Andrews et al 2004, Heron et al 2004) addressed the role of early exposures, e.g., prior to 3, 4 or 6 months of age, comparing those who received thimerosal-containing vaccines by a given age vs. those who did not and hence may have received them at a later age. In these studies, most adverse developmental outcomes were less prevalent in those receiving the early vaccines, and several were significantly less prevalent, raising the possibility of a 'healthy vaccinatee effect' (similar to the well-characterized 'healthy worker effect' found in occupational studies). In the CDC study (Verstraeten et al 2003), a relatively large percentage of births (~20%), including many who would be considered at increased risk for autism based on current knowledge (low birth weight, maternal perinatal conditions, malformations of genetic or chromosomal origin), were excluded. In a multi-factorial developmental disorder, those with predisposing conditions may be most vulnerable to a later insult. Thus, the exclusion criteria may have lowered statistical power and introduced selection bias.

Conclusions: Of published studies meeting pre-established minimal criteria, none supports an association between thimerosal-containing vaccines and autism. However, in each of the null studies, methodologic weaknesses limit the conclusions that can be drawn. The strength of evidence in support of the hypothesis that thimerosal-containing vaccines play no role in autism may have been overestimated in previous reviews and editorials. Bias and confounding, including that due to indications for early vs. later vaccine administration, should be addressed in future studies.

134.81 81 Validating a Japanese Version of the Ritvo Autism and Asperger's Diagnostic Scale. K. Matsumoto*[1], K. Tsuchiya[1], M. Tsujii[2] and R. A. Ritvo[3], (1)*Hamamatsu University School of Medicine*, (2)*Chukyo university*, (3)*Yale University School of Medicine*

Background: Diagnosing Autism and Asperger's disorder among adults has been a concern in clinical settings. We reported potential efficacy and limitation of a preliminary Japanese version of the Ritvo Autism and Asperger's Diagnostic Scale (RAADS, Ritvo et al., 2007) in IMFAR 2008. Although internal consistency of the Japanese version of the RAADS (RAADS-J) was confirmed, there were not statistically significant differences between 6 Autism Spectrum Disorders (ASD) and 49 control participants in 45 out of 80 items, including 21 items that have successfully discriminated ASD from non-ASD individuals in the previous report. Taking these limitations into account, the Japanese translation needs to be revised, since literal translation of some social expressions, such as "I've got you under my skin," might have compromised comprehensibility of the items.

Objectives: We revised the Japanese version of the RAADS, and tested the reliability and validity of the scale.

Methods: The preliminary version of the RAADS-J was revised so that people aged 18 and over can understand the meaning without confusing or difficulties, with thorough considerations on cultural perspectives of the Japanese social and colloquial expressions. It was distributed to a hundred individuals with ASD, who participated in the public event aiming for networking of adults with ASD in which one of the authors (MT) attended as an instructor. Fifty volunteers of students from two Universities were also recruited as control. In addition, 60 in-patients with three different psychiatric disorders (i.e., schizophrenia, major depression, and anxiety disorders) in the hospital affiliated to Hamamatsu University School of Medicine voluntarily participated in the study. All participants were asked for completion of the

revised RAADS-J twice to check test-retest reliability as well as Autism–Spectrum Quotient Japanese version (AQ-J) to test the criterion-related validity.

Results: With the revised version of the RAADS-J, we successfully discriminate adults with ASD from non-ASD adults, as well as from adults with other psychiatric disorders.

Conclusions: Same as the original RAADS, the RAADS-J is also useful as a clinical scale to assist identification of Autism and Asperger's Disorder in adults.

134.82 82 Two-Stage Autism Screening. R. L. Hefter*, M. A. Gernsbacher, E. K. Schweigert and H. H. Goldsmith, *University of Wisconsin-Madison*

Background: The Modified Checklist for Autism in Toddlers (M-CHAT, Robins, Fein, Barton, & Green, 2001) is a widely used early autism screener; however, it is rarely followed up with measures for school-age children, such as the Social Communication Questionnaire (SCQ; Rutter et al., 2003) or the Social Responsiveness Scale (SRS; Constantino et al., 2003). Such two-stage screening would best assess the M-CHAT's predictive power.

Objectives: The primary goals of the study were to (1) complete a two-stage screening of twins born from 1998-2004 who were recruited from birth records or via statewide case-finding; (2) consider use of both threshold and full range M-CHAT scores in predicting later SCQ and SRS scores; and (3) identify specific items indicative of false positive M-CHAT scores.

Methods: Recruitment occurred in a step-wise fashion. First, mothers of >3000 twins from a statewide, unselected population born from 1998-2004 completed items similar to the six critical M-CHAT items when the twins were between 2 and 3 years of age. Second, twin pairs in which at least one of the twins (1) had at least two endorsed M-CHAT items (n=14 pairs) or (2) received subsequently a community autism spectrum diagnosis, regardless of M-CHAT score (n=16 pairs) were invited to participate in another screening phase when the twins were at least 4 years of age. The SRS and SCQ composed the second phase of screening.

Results: Of 29 individual twins scoring at or above the published threshold of two endorsed M-CHAT items, 12 did not meet or exceed threshold on either the SCQ or the SRS (with the SRS cutoff of 76 T-score). Shifting to a higher threshold of at least three endorsed MCHAT items (which reduced the above-threshold N from 29 to 11), only two children did not meet threshold on either the SCQ or the SRS, and the other nine met threshold on both the SCQ and SRS. For the threshold of two M-CHAT items, we determined that M-CHAT items assessing interest in other children, sharing, and following gaze most frequently characterized children who would later be designated as "false positives," whereas the item assessing eye contact contributed to "true positive" outcomes. Total M-CHAT scores were moderately correlated with both the SCQ (r=.64) and SRS (r=.53) for males (n=42), but not for the much smaller group of females (SCQ, r=.34; SRS, r=.15). These correlations suggest that the M-CHAT is predictive across the range of scores and may be useful as a dimensional measure. Limitations of sample size, lack of follow-up of children with sub-threshold M-CHAT scores, and possible age-dependence of findings will be discussed. A second follow-up of the sample with the Autism Diagnostic Observation Scale will also be described.

Conclusions: A slightly higher M-CHAT threshold than is usually employed may minimize false positives, and the full range of M-CHAT scores may be predictive of later SCQ and SRS scores. Endorsement of particular M-CHAT items may be associated with false positive screening outcomes.

134.83 83 The Influence of Gender and Speech on Autism Symptomatology as Measured by the ADI-R. A. V. Hall*[1], R. K. Abramson[2], S. Ravan[2], M. L. Cuccaro[3], J. R. Gilbert[3], M. A. Pericak-Vance[3] and H. H. Wright[2], (1)*Univ. S. Carolina Sch. Public Health*, (2)*University of South Carolina School of Medicine*, (3)*University of Miami Miller School of Medicine*

Background: Autistic Disorders (AD) is characterized by a higher prevalence in males with a male/female ratio of 4:1. The ADI-R is the gold standard instrument used for research and clinical diagnosis of AD (Lord, 1995). Individuals are diagnosed with AD if they meet criteria in all three domains of the ADI-R: social, communication, and repetitive Stereotyped Behaviors (RSB). Symptom differences between males and females diagnosed with AD by the ADI-R are not always obvious. This study examines differences between the ADI-R domains in males and females with AD.

Objectives: To evaluate symptom differences in persons diagnosed with AD using the ADI-R domains in males and females who are verbal, verbal with difficulty (VWD), and non verbal.

Methods: The study included 266 subjects (207 males, 59 females) with an ADI-R diagnosis of AD. Level of speech was based on ADI-R criteria for verbal vs. nonverbal. Multivariate ANOVA used to evaluate the effect of gender and level of speech for the Social (B1, B2, B3, B4), Communication (C1, CV2, CV3, C4) and RSB (D1, D2, D3, D4) subdomains and domain total scores. For the Communication, subdomains CV2 and CV3 were omitted for nonverbal or VWD individuals.

Results: The omnibus multivariate test on the ADI-R Social domain showed there were no overall gender effects. However, there was an effect for level of speech, (F=3.048, p=0.002). Between subjects analysis showed a main effect for level of speech and the Social domain and 2 of the 4 subdomains: B3 ($F_{(1,265)}$=4.491, p=0.012), B4 ($F_{(1,265)}$=10.416, p=0.000) and Social total score ($F_{(1,265)}$=7.080, p=0.001). Post-hoc comparisons using Scheffe indicate there was a significant difference between verbal and nonverbal groups on B3 (lack of shared enjoyment), B4 (lack of socio-emotional reciprocity), and overall social score. The verbal group also differed significantly from the VWD group on B4 (lack of socio-emotional reciprocity). In the Communication domain, there was significant gender difference for VWD group on C4 ($F_{(1,37)}$=5.655, p=.023) with females exhibiting less deficits in social play. The verbal group showed significant differences on the CV2 (conversation skills) subdomain, $F_{(1,174)}$=3.898, p=0.050), with females exhibiting less deficits. There were no gender differences in the Nonverbal group. The omnibus multivariate test on the ADI-R RSB domain indicated no overall gender effects. There was an effect for level of speech, (F=8.659, p=0.000). The between subjects analysis showed a main effect for level of speech and the RSB domain and the 3 of the 4 subdomains: D1 ($F_{(1,265)}$=5.840, p=0.003), D2 ($F_{(1,265)}$=20.129, p=0.000), D4 ($F_{(1,265)}$=5.488, p=0.005) and RSB total score ($F_{(1,265)}$=6.410, p=0.002). Additionally, there were significant differences between the verbal and nonverbal groups on D1 (preoccupations), D2 (routines), D4 (preoccupations with objects) and the overall RSB score.

Conclusions: The diagnosis of an ASD by ADI-R represents a complex pattern of behaviors with males and females achieving diagnosis frequently by different sets of symptoms, influenced strongly by speech. This profile of symptoms more prevalent in females than males needs to be replicated in a larger sample and has implications for shaping early intervention strategies in males and females.

134.84 84 The Effects of Age, Gender, Race, and Level of Speech on Problem Behaviors in a Sample of Children and Adolescents.

H. H. Wright*[1], A. V. Hall[2], S. Ravan[1], M. L. Cuccaro[3], J. R. Gilbert[3], M. A. Pericak-Vance[3] and R. K. Abramson[1], (1)*University of South Carolina School of Medicine*, (2)*Univ. S. Carolina Sch. Public Health*, (3)*University of Miami Miller School of Medicine*

Background: As we learn more about Autistic Disorder (AD), we have come to understand that some behaviors change with age while others remain the same. The Aberrant Behavior Checklist (ABC) is commonly used to assess a set of problem behaviors in children and adolescents with AD. Change in problem behaviors over the lifespan is an area of emerging importance in evaluating need for services as the number of individuals identified with AD has increased significantly.

Objectives: To evaluate the effects of age, gender, race, and level of speech on problem behaviors in a sample of children and adolescents with AD as measured by parent report on the ABC.

Methods: Parents completed the ABC for 244 children and adolescents with a current ADI-R diagnosis of AD. Level of speech was based on ADI-R criteria for verbal vs. nonverbal. Multivariate ANOVAs were used to evaluate the effects of age (under 13 years, n=200; 13 years and older, n=44), race (Caucasian, n=181; non-caucasian, n=63), gender (male, n=192; female, n=52) and level of speech (verbal, n=162; nonverbal, n=82) on the ABC total and subscale scores.

Results: There were no significant differences in Total Score, Irritability, Lethargy, Stereotypy, Hyperactivity, or Inappropriate Speech for age or gender alone. Caucasians' scores were significantly higher than non-caucasians for Irritability, $F_{(1, 243)}$=3.908, p=0.049, hyperactivity, $F_{(1, 243)}$=5.974, p=0.015, and total score, $F_{(1, 243)}$=5.979, p=0.015. There was a race by age

interaction effect, with non-caucasians scoring significantly lower on Hyperactivity, $F_{(1,243)}$=6.381, p=0.012 than the other groups. Verbal individuals scored significantly higher on Irritability, $F_{(1,243)}$=7.703, p=0.006 and Inappropriate Speech, $F_{(1,244)}$=35.192, p=0.000).

Conclusions: From this study we can conclude that age and gender do not affect the parent perceived severity of problem behaviors for children or adolescents as measured by the ABC. However, parental perceptions of problem behaviors differed. Overall Caucasian parents report more problems with irritability and hyperactivity than reported by non-caucasian parents. The interaction effect showed that non-caucasian adolescents were rated the least hyperactive. Parents also perceived their verbal children as significantly more irritable than their nonverbal children. The differences in parent perceptions by race and by speech need to be evaluated independently in a larger study to determine whether these are true differences or differences based on cultural perception. This will help to determine more appropriate interventions and supports to families.

134.85 85 Diagnostic Utility of Adaptive Behavior in Children with a Referral Question of ASD. E. H. Sheridan*, E. M. Griffith and S. Mrug, *University of Alabama at Birmingham*

Background: Impairment in adaptive functioning is a hallmark feature of Autism Spectrum Disorders (ASD). Previous research suggests that the Vineland Adaptive Behavior Scales (VABS) may have diagnostic utility when diagnosing ASD. Furthermore, the most recent version of the VABS, the Vineland-II, holds promise to obtain a more sensitive measure of developmental level in individuals with ASD in early childhood and across the lifespan. However, the diagnostic utility of the Vineland-II and the specific relationship between adaptive functioning and autistic symptomatology have not been investigated. Objectives: To examine the relationship between adaptive functioning (as measured by Vineland-II) and autistic symptomatology (as measured by Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview-Revised (ADI-R)) and to determine if the Vineland-II adds to the prediction of diagnostic outcome over and above that of the ADOS and ADI-R for individuals with a referral question of ASD. Methods: Data were pooled from the medical records of 120 children evaluated at a university-based autism clinic who received a diagnosis of Autistic Disorder (N=30), Pervasive Developmental Disorder-Not Otherwise Specified (N=30), Developmental Delay (N=30), or Language Disorder (N=30). All children were evaluated with ADI-R, ADOS, and Vineland-II measures. Pearson Product Moment Correlations will be conducted to investigate the relationships between Vineland-II Communication and Socialization scores and Communication and Social scores on the ADI-R and the ADOS. Additionally, hierarchical logistic regression analyses will examine the incremental diagnostic utility of Vineland-II above ADOS and ADI-R in predicting ASD diagnoses. Results: Data will be presented to elucidate the relationships between adaptive behavior and autistic symptomatology in children with a referral question of ASD. Additionally, data will be analyzed to determine if the Vineland-II scores improve diagnostic accuracy beyond the current gold standard of ADOS and ADI-R diagnostic evaluations. Conclusions: While the Vineland-II holds promise as a more sensitive measure of developmental level in children with ASD, it is too recent to have been widely studied and there have been no published studies in ASD using this measure to date. The present study will provide important information on how the Vineland-II scores relate to autistic symptom presentation across a variety of ASD and non-ASD developmental diagnoses. Ultimately, the identification of specific diagnostic thresholds in measures of adaptive behavior may help distinguish children with ASD from those with other developmental delays. This study takes the first step in this direction by assessing the incremental predictive utility of adaptive behavior in a comprehensive assessment of individuals with a referral question of ASD.

134.86 86 The Passage Rate on Each Item of the M-CHAT for Children with ASD: The Cultural Differences Between Japan and USA. N. Inada*, T. Koyama and Y. Kamio, *National Center of Neurology and Psychiatry, Japan, National Institute of Mental Health*

Background: The Modified Checklist for Autism in Toddlers (M-CHAT) is a yes/no 23-item parent-report developmental screener designed to detect Autism Spectrum Disorders (ASD). Its Japanese version have been developed and validated; however, to introduce the M-CHAT in Japan further, we need to consider how Japanese childrearing culture influences on parent-report.

Objectives: To investigate how much the passage rate on each item of the M-CHAT in

children with/without ASD differs between Japan and USA.

Methods: The participants were 2063 children with non-ASD and 27 children with ASD who received the M-CHAT at 18-month health check-up in Japan. Children with ASD were diagnosed at the age of 2 using DSM-IV-TR and Childhood Autism Rating Scale-Tokyo Version (CARS-TV). We calculated the passage rate on each item of the M-CHAT for children with ASD/non-ASD and compared with those in the USA counterparts (Robins et al, 2001).

Results: For children with non-ASD, the passage rates on each item were very similar bothb in Japan and USA. For children with ASD, however, the Japanese children passed 20% higher compared to USA children on 14 items. Especially, 5 items out of the 14 items showed 40% higher: "interest in other children" (Japan vs. USA, 88.9% vs. 41.0%), "response to name" (85.2% vs. 35.9%), "pointing-following" (81.5% vs. 25.6%), "attract parents' attention" (77.8% vs. 23.1%), and "concern with hearing" (100.0% vs. 46.2%). On the other hand, the Japanese children with ASD passed less on the item "social reference" (51.9% vs. 82.1%).

Conclusions: It might be difficult for Japanese parents to give definite negative answers to their children's mild or subthreshold abnormal behaviors. To screen Japanese children with ASD using the M-CHAT effectively, we may need to apply grading answers instead of yes/no one, like Wong et al (2004) did in Chinese version.

Sponsor: RISTEX (Research Institute of Science and Technology for Society)

134.87 87 Adding ESCS Measures of Initiating and Responding to Joint Attention to the M-CHAT. S. Anderson*, M. Khowaja, D. L. Robins and L. Adamson, *Georgia State University*

Background: The American Academy of Pediatrics recommends universal autism-specific screening. Differentiating autism spectrum disorders (ASD) from language or global developmental delay (DD) is challenging due to symptom overlap in young children. The Modified-Checklist for Autism in Toddlers (M-CHAT; Robins et al., 1999) identifies children at risk for ASD, but has poor to moderate positive predictive value, indicating that some cases who screen positive on the M-CHAT have a non-ASD DD. Studies show that children with ASD show more impairment in initiation of joint attention (IJA) and in response to joint attention bids from others (RJA) than children with DD.

Objectives: The current study examines whether the combination of M-CHAT and Early Social Communication Scales (ESCS; Mundy et al., 2003) IJA and RJA scores differentiate ASD from DD in a sample of toddlers who screened positive on the M-CHAT better than M-CHAT alone.

Methods: Thirty-one children who screened positive on the M-CHAT during a well-child checkup were recruited from a larger study. Of these children, 11 (7 males; mean age=23.67 months, *SD*=4.40) were subsequently diagnosed with DD and 20 (20 males; mean age=24.83 months, *SD*=3.37) were diagnosed with an ASD. Mean age was not significantly different between groups, $t(29)=-.823$, $p=.417$. Those who screened positive on the M-CHAT and subsequent follow-up interview completed the ESCS and a diagnostic evaluation, which included the Mullen Scales of Early Learning (MSEL; Mullen, 1995) to measure cognitive development. Analyses using M-CHAT critical score were similar to results using M-CHAT total score, so only total score analyses are reported.

Results: M-CHAT scores were not significantly different between the ASD group ($M=7.90$, $SD=2.75$) and the DD group ($M=6.27$, $SD=4.10$), $t(29)=-1.32$, $p=.197$. However, the ASD group demonstrated less IJA ($M=6.45$, $SD=8.80$) than the DD group ($M=18.36$, $SD=11.11$), $t(29)=3.29$, $p=.003$, and similarly less RJA ($M=12.30$, $SD=19.44$) than the DD group ($M=57.05$, $SD=23.10$), $t(29)=5.74$, $p=.000$. Binary logistic regression analyses were conducted to classify participants as ASD or DD. M-CHAT alone correctly classified 71% of the participants. The addition of ESCS IJA and higher level RJA scores classified 87.1% of the participants, a significant improvement over M-CHAT alone, $\chi^2(3)=19.95$, $p=.000$. Neither IJA nor M-CHAT total scores were significant independent predictors of diagnostic group membership, though higher level RJA score was significant, $Exp(B)=.916$, $SE=.04$, $p=.02$. When level of cognitive development was controlled using the Mullen early learning composite standard score, 90.3% of the sample was correctly classified, $\chi^2(4)=20.51$, $p=.000$; neither M-CHAT nor ESCS scores were significant

independent predictors once cognitive level was included.

Conclusions: Adding ESCS JA measures to the successfully improved differentiation between ASD and DD. Given that ESCS JA measures help differentiate ASD DD, a second level screen after a positive M-CHAT may be useful to determine which cases should be referred to ASD specialists. A combination of M-CHAT and ESCS may reduce over-referrals to ASD specialists, while still maintaining very successful early detection of autism spectrum disorders.

134.88 88 Parent-Reported Concerns in Early Development that may Predict Specific Pervasive Developmental Disorder (PDD) Diagnoses. C. A. McMorris*[1], J. H. Schroeder[2] and J. Bebko[2], (1)*York University, Toronto*, (2)*York University*

Background: Families of children with a Pervasive Developmental Disorder (PDD) have continually reported frustration with the process of diagnosing their child (Howlin & Moore, 1997). Despite reports of early initial concerns, generally between 18 and 24 months, the diagnostic process often takes several months or years. The process often involves multiple visits to a variety of different professionals with various diagnoses having been given. Parents typically report early concerns related to joint attention, imitation, gestural use, and babbling in early development (De Giacomo & Fombonne, 1998). However, it is unclear as to whether specific concerns are predictive of a later diagnostic category of PDD (i.e., Asperger Syndrome, Autism, PDD-NOS).

Objectives: Update our understanding of the experiences of families during the diagnostic process, specifically related to concerns in early development, which result in later PDD diagnoses.

Methods: Family members of children were invited to complete an internet questionnaire related to their child's diagnostic history, through the Autism Spectrum Disorder-Canadian American Consortium (ASD-CARC) website. Questions included "How old was your child when you first became concerned?", "What was of particular concern to you?" and "Who first recommended that your child be assessed for an Autism Spectrum Disorder?"

Results: Preliminary frequency analysis of the first twenty parent responses continued to reveal a discrepancy between the average age children received a diagnosis (*M* = 5 yrs 2 months) and the age at which family members had initial concerns (*M* = 2 yrs). The most common concerns reported by parents were: 1) Lack of language development (57%); 2) Repetitive or rigid behavior (43%); and 3) Lack of imitation (43%). Frequency of other concerns, such as self injurious behavior and violent behavior, will also be reported, as well as an analysis of age of diagnosis and type of concerns for each diagnostic category (Autism, Asperger Syndrome, PDD-NOS). Data collection is ongoing.

Conclusions: Understanding the experiences of families throughout the diagnostic process as well as concerns in early development compared to previous studies (Howlin & Asgharian, 1999; Gray & Tonge, 2001) can contribute not only to earlier identification of PDDs but may also help to clarify appropriate differential diagnostic procedures for professionals.

134.89 89 Age at First Diagnosis of An Autism Spectrum Disorder in Different Regions of Canada. H. Ouellette-Kuntz[1], H. Coo*[1], M. Lam[1], C. T. Yu[2], M. E. S. Lewis[3], D. Dewey[4], F. Bernier[5], M. Breitenbach[6], A. Chudley[7] and J. J. A. Holden[1], (1)*Queen's University*, (2)*University of Manitoba and St. Amant Centre*, (3)*University of British Columbia*, (4)*University of Calgary*, (5)*Alberta Children's Hospital*, (6)*Department of Education and Early Childhood Development*, (7)*University of Manitoba*

Background:

Early diagnosis of autism spectrum disorders (ASDs) reduces family stress, empowers parents to make choices such as seeking genetic counseling, and may lead to better treatment outcomes. There are no empirical data on the age at which Canadian children are first diagnosed with an ASD.

Objectives:

To examine: 1) the age at which children are first diagnosed with an ASD in different regions of Canada; 2) whether the age at diagnosis is decreasing; and 3) the association between specific factors and age at diagnosis.

Methods:

The data for this analysis were collected as part of a Canadian surveillance program for ASDs (National Epidemiologic Database for the Study of Autism in Canada: NEDSAC). Population-based surveillance of diagnosed cases of ASD among children has been ongoing since 2002 in Manitoba

and Prince Edward Island (PEI), and since 2003 in Newfoundland/Labrador and Southeastern Ontario. From 2002 to 2007 data were also collected on children diagnosed with an ASD at three referral centres in Vancouver, British Columbia (BC), and from 2003 to 2006 on children with an ASD identified through various sources in Calgary, Alberta. The sample for this analysis included children living in one of the surveillance regions who were first diagnosed with an ASD between 1997 and 2005. For the first two objectives, we included data from Manitoba, Southeastern Ontario, PEI, and Newfoundland/Labrador. We used the Kruskal-Wallis test to compare age at diagnosis among regions, and the Spearman's rank correlation to examine intra-regional trends by three-year period of initial diagnosis. We included data from all six geographic areas to examine factors related to age at diagnosis. Due to small cell counts for some variables in Calgary, Southeastern Ontario, PEI, and Newfoundland/Labrador, we pooled the data from those four regions (=four combined regions). The multiple imputation procedure in SAS was used to impute values for missing data, and generalized linear regression models were fit for BC, Manitoba, and the four combined regions.

Results:

There were significant differences in the age at first ASD diagnosis among the regions ($p<.001$), ranging from a median of 39 months in Newfoundland/Labrador to 55 months in Southeastern Ontario. No temporal decreases in age at diagnosis were found, and in Southeastern Ontario the age at diagnosis increased significantly ($p=.004$). Asperger disorder, PDD-NOS, birthplace outside Canada, being adopted, being female, and Aboriginal identity were all associated with a later age at diagnosis in one or more regions. No significant associations were found between age at diagnosis and urban/rural residence or household income.

Conclusions:

Our findings suggest that Canadian children with an ASD are not being diagnosed at as young an age as the literature suggests they could be. Future studies should include a broader range of factors that may affect age at diagnosis, such as waiting times for assessment. Such research will complement efforts to increase awareness of ASDs among parents and professionals, in the hopes that this will lead to earlier detection and access to treatment and support for children with ASDs and their families.

134.90 90 Screening for Autism and Developmental Disorders in Toddlers from a Lower Socio-Economic Strata Using the MCHAT and ASQ; Fail Rates by Demographic Characteristics. G. C. Windham*[1], K. S. Smith[1], N. J. Rosen[1], J. K. Grether[1], R. B. Coolman[2] and S. J. Harris[2], (1)*California Department of Public Health*, (2)*Santa Clara Valley Health and Hospital System*

Background:

The American Academy of Pediatrics recommends early screening for developmental disabilities (DDs), including autism spectrum disorders (ASD). Surveillance of ASD has consistently shown lower prevalence rates among Hispanics than Whites. To investigate possible reasons for this, including limited health care access, we initiated a screening program in a county health system serving a primarily Hispanic population.

Objectives:

Screen all children born in 2006 attending well-child pediatric visits between 16-30 months of age at two clinics and compare fail rates to other populations and by demographic characteristics.

Methods:

The Modified-Checklist for Autism in Toddlers (MCHAT) and the Ages and Stages Questionnaire (ASQ) were given to parents of children who fit our criteria, with a choice of English or a Spanish translation. These were scored on-site by our staff, and results provided to pediatricians to inform their exams, discussion with parents, and decision to refer or continue monitoring. We linked our screened population to the clinic data base and the California birth certificate file to obtain demographic data including maternal race, age and education, and child's race and age at screening. We calculated MCHAT fail rates for first screens only and for any screen and then compared them by ASQ fail rates and by demographic characteristics, using the chi-square test (p-value <0.05 indicating statistical significance); multi-variate modeling will also be conducted

Results:

We linked 92% of the screening records to birth certificates, yielding data on 2,010 screens, representing 1,518 individual children. Overall, 21% of screens resulted in a failed MCHAT and 32% in a failed ASQ (on any domain). Examining the first screens only, 21% of children failed the MCHAT, of which, half also failed the ASQ; 32% failed the ASQ communication domain and 18% the social domain. Children of Hispanic race/ethnicity (81% of the sample) were significantly more likely to fail the MCHAT than Whites; 22.6% vs. 13.3 % respectively. Also, the 60 percent of children with Spanish language screens had a significantly higher fail rate (25.1%) than those with English (16.0%). MCHAT fail rates were also higher among children with less educated mothers (p=0.07) and somewhat higher among younger mothers, but not significantly.

Conclusions:

This sample's MCHAT fail rate is about twice that found in other studies of children of a similar age. This may be due to a higher prevalence of DDs in this lower socio-economic population, or to differences in interpretation of the instruments by these parents. The higher fail rate observed among Hispanic children and less educated mothers is opposite the pattern typically seen for ASD rates. However, we do not yet know which children will be diagnosed with an ASD or DD. Our results indicate that screening a low SES, Hispanic population can be conducted but may require more clinical resources to facilitate administration and to conduct follow-up on a higher proportion. The surveillance we ultimately complete in this county will determine if screening helped identify more children with ASD than in the prior year.

134.92 92 Autistic Diagnosis in China – An Investigation in North China Over 16 Years. C. Y. Wang*, *Nankai University*

Background: Since four children were first diagnosed with autism spectrum disorders (ASDs) in China in 1982, the number has been growing fast. However, there is very few large scale epidemiological investigation about the prevalence of ASDs and there is no such a registry for autism to collect and store all the inpatient data from all the public hospitals in China. We collected and analyzed all the hospital records of children diagnosed with ASDs in north China from 1993 to 2008.

Objectives: This is an attempt to investigate the prevalence, diagnosis and characteristics of ASDs in China since early 1990s.

Methods: The data we collected about the children diagnosed with ASDs in North China since 1993 include: date of birth, date of being diagnosed, IQ, Children Intelligence Development Index, Clancy Behaviour Scale, SM, Child Behavior CheoKlist (CBCL), Sensory Integration Rating Scale, Children Temperament Scale (CTS), Toddler Temperament Scale (TTS), Gesell Development Schedules (GDS), DSC, etc., which are the most common diagnostic methods widely used in China over the 16 years.

Results: From March 1993 to September 2008, there have been 1886 children diagnosed with ASDs in north China (northeast China, Shandong province, Hebei Province, Shanxi Province, Tianjin mainly), including 1441 boys and 417 girls (the ratio is 3.4556 : 1). The average age when first being diagnosed with ASDs is 38.34 months. To our surprise, there are 57 infants younger than 12 months diagnosed with ASDs. Between 1993 to end of 1999, there were only 85 children diagnosed with ASDs. 1285 children were diagnosed with Clancy Behaviour Scale, and their mean is 15.210.

Conclusions: The results of this study supported the former research on the ratio of male to female and incidence rate. The autistic children population grew very fast in the past decades and their diagnosed ages became younger, so there is an urgent need for early diagnosis and intervention.

134.93 93 Trends in Prevalence of ASD Diagnosis in a Large Health Care Population in the U.S. P. Bernal*, L. Croen and C. Yoshida, *Kaiser Permanente*

Background: The reported prevalence of autism spectrum disorders (ASD) has increased dramatically over recent decades. Although recent studies reflect a 10-fold increase compared to studies of a half-century ago that chiefly targeted autistic disorder, most of the newer studies also included individuals with Asperger's and PDD-NOS. There is a scarcity of reports of trends in the prevalence of ASD in large health care populations in the U.S..

Objectives: To present trends in a large health care population from 2001 to 2008 in: (1) ASD prevalence in children aged 0-18; (2) ASD prevalence by age group and gender; and (3) prevalence of subcategories of ASD diagnoses.

Methods: We studied children 0-18 years of age who were enrolled in Kaiser Permanente (KP) in northern California during the period 2001 through 2008. KP is an integrated, group-model, nonprofit health plan serving over 3.2 million residents of northern California. KP members are demographically similar to the population residing in the 14-county area served by the health plan. All inpatient and outpatient diagnoses are recorded in the KP electronic medical record system. All children with at least one outpatient ASD diagnosis (Autism [ICD-9-CM) 299.0]; Asperger's disorder or Pervasive Developmental Disorder-Not Otherwise Specified [ICD-9-CM 299.8]) recorded in electronic medical records were identified. Prevalence of ASD was calculated for current members in the target age range for each of the following years (July-June): 2001, 2004, 2005, 2006, 2007, and 2008.
Results: There were 700,561 members aged 0-18 years in 2001 and 804,181 in 2008. (1) From a base of 2,699 children aged 0-18 with any ASD diagnosis in 2001 (prevalence: 3.9/1,000), the prevalence grew by 15% per year through 2005, and by 23% from 2005-2006 and 20% from 2006-2007. From 2007-2008, the prevalence grew by only 5% to a total of 7,479 children with any ASD diagnosis (current prevalence: 9.3/1,000). (2) Since 2001, the prevalence has remained highest in the 5-9 (2008: 12.5/1,000) and 10-14 (2008: 10.7/1,000) age groups. Since the first KP ASD evaluation and diagnostic center opened in 2004, there has been a more rapid increase in the prevalence of ASD in the 0-4 age group (2005: 3.1/1,000; 2008: 5.2/1,000). The relative prevalence between boys and girls has remained constant since 2001,with girls constituting 19% of the total throughout the time period (2001: boys = 6.1/1,000, girls = 1.5/1,000; 2008: boys = 14.1/1,000, girls = 3.4/1,000). (3) The proportion of Autism vs. Asperger's /PDD-NOS diagnoses changed only slightly over the period from 54% (2.1/1,000) vs. 46% (1.8/1,000) in 2001 to 60% (5.6/1,000) vs. 40% (3.7/1,000) in 2008.
Conclusions: In general, the trends in ASD prevalence in this large health care population are similar to those reported in previous epidemiologic studies. The most recent data suggest that there may be a plateau in the increase in ASD diagnoses. The increase over time in ASD prevalence in the 0-4 age group may indicate a change towards earlier detection.

134.94 94 Early Behaviors Linked to Later Autism Spectrum Disorders in NICU Infants. J. M. Gardner*[1], B. Z. Karmel[1], L. D. Swensen[1], I. L. Cohen[1], E. M. Lennon[1], P. M. Kittler[1], R. L. Freedland[1], M. J. Flory[2] and E. London[2], (1)*NYS Institute for Basic Research in Developmental Disabilities*, (2)*New York State Institute for Basic Research in Developmental Disabilities*

Background:

Infants with obstetric/neonatal complications such as those seen in neonatal intensive care units (NICUs) appear to have 3 to 4-fold risk for Autism Spectrum Disorders (ASDs). Our longitudinal studies with medically-at-risk NICU infants from birth follow development of regulatory influences on multiple domains including attention, motor skills, social communication, temperament, and cognition. We previously reported archival demographic, medical, neonatal neurobehavior (NB) and attention data on NICU infants later diagnosed with ASDs. This report further analyzes this set of data on additional tasks in later infancy to identify patterns in neurodevelopment specific to these infants.

Objectives:

To identify potential behavioral markers and precursors to ASD in early infancy.
To posit potential mechanisms underlying neurodevelopment of behaviors across ASD-specific domains.

Methods:

NICU infants were evaluated prior to hospital discharge and followed every few months from birth to 5 years. Data included information about medical conditions and demographics at birth, early neurological insult, and a variety of behaviors in multiple domains. This report compares NICU infants later diagnosed with ASD (n = 33; 19 by co-author ILC, 14 by other sources) to controls (n = 134; matched on gender (81% male), gestational age at birth (23-41 weeks) and year of birth (1994-2006)) from birth to 2 years. Behaviors include neonatal NB, arousal modulation of visual attention (AMA), focused attention and distractibility, exploration in a novel environment, and cognitive and motor performance.

Results:

In analyses controlling severity and maternal education, ASD infants exhibited behavioral deficits starting in the newborn period. Their neonatal NB showed more visual asymmetry, tone differences between arms and legs, and less decrease in number of abnormalities at 1 month (p's < .01). They had poorer AMA out to 4 months (p < .001), with more attention to faster stimuli (like younger or cocaine-exposed infants). They showed attention problems and less habituation to distractors during a focused attention task at 10 and 13 months; fewer referenced examiner (p < .07) or looked at toys (p < .003), and many spent most of the time looking at distractors (p < .10). Their behavior in a novel environment (13-25 months) appeared to indicate repetitive stereotypic movements, lack of toy play, and an atypically positive approach to a 2-ft robot. Their scores on BSID-II MDI and PDI declined as early as 7-10 months, which typically only occurs in infants with the most severe pathology.

Conclusions:

Infants later diagnosed with ASD may form a distinct sub-group within NICU babies, with atypical visual, motor, and regulatory development. They have a unique behavioral profile, with slower resolution of neonatal problems and development, atypical visual function, lack of toy play, and motor as well as cognitive involvement starting much earlier than expected. Studies of NICU infants should provide opportunities to observe and identify potential markers and precursor behaviors at much younger ages than symptoms are seen or ASD diagnosed. Earlier identification is important for earlier intervention potentially improving long-term outcome.

134.95 95 Comparison of Diagnostic Classifications Using the Original and Revised ADOS Algorithms in Individuals with Fragile X Syndrome. S. W. Harris*[1], B. Goodlin-Jones[1], E. Hare[1], A. Wesnousky[1], L. Cordeiro[1] and R. Hagerman[2], (1)*M.I.N.D. Institute, University of California at Davis Medical Center*, (2)*UC Davis*

Background: The Autism Diagnostic Observation Schedule (ADOS) is a widely-used, gold standard tool for the diagnosis of autism and autism spectrum disorders. It consists of various items which are administered directly with individuals in a 30-45 minute session. These items are then used to code domains of Language and Communication, Reciprocal Social Interaction, Imagination, and Stereotyped Behaviors and Restricted Interests. Items from the Language and Communication, and Reciprocal Social Interaction domains are used to code the original ADOS algorithm, which provides overall diagnostic categories of autism or autism spectrum. Gotham et al (2007) reported on a revised version of the algorithm which was developed for modules 1 through 3, and also incorporates items from the Stereotyped Behaviors and Restricted Interests domain for the overall scoring algorithm.

Objectives: We were interested in seeing whether the ADOS classifications of individuals with fragile X syndrome would change when using the new algorithm, what types of changes would be seen, and with what frequency.

Methods: We used an existing sample of 304 individuals with fragile X syndrome who had been seen previously for research studies utilizing the ADOS. We re-scored the ADOS modules 1, 2 and 3 using the new version of the algorithm reported by Gotham et al. (2007), and compared the results of the classification with the revised algorithm to those of the original algorithm.

Results: We re-scored ADOS administrations using the revised algorithms for 304 individuals (246 males, 58 females). The subjects ranged in age from 1 to 50 years (mean=10, ± 7). Of the 304 cases, 89 were module 1 (29%), 126 were module 2 (41%), and 89 were module 3 (29%). Overall, 93 of 304 cases (30%) showed some type of change in their overall ADOS classification. Specifically, changes seen were non-ASD to autism spectrum (n=14), non-ASD to autism (n=9), autism spectrum to autism (n=58), autism spectrum to non-ASD (n=7), and autism to autism spectrum (n=5).

Conclusions: A significant number of the 304 cases analyzed showed some type of change in their ADOS classification, and changes were seen in both 'directions'. The most frequent change shown was from autism-spectrum to autism (58/93 cases, 62%), which may suggest that the addition of the repetitive behavior items to the new algorithm has a significant influence for the classification of autism in the fragile X population. These findings further support the need for using multiple tools for the diagnosis of autism (see Risi et al. 2006 and Harris et al. 2008)

134.96 96 The Autism Birth Cohort Study - Status and Future Plans. P. Surén*[1], M. Bresnahan[2], M. Hornig[2], K. K. Lie[1], T. Reichborn-Kjennerud[1], S. Schjølberg[1], D. Hirtz[3], P. Magnus[1], E. Susser[2], C. Stoltenberg[1] and W. I. Lipkin[2], (1)*Norwegian Institute of Public Health*, (2)*Columbia University*, (3)*National Institutes of Health*

Background: The Autism Birth Cohort (ABC) Study is a scientific collaboration between the Norwegian Institute of Public Health, the Mailman School of Public Health at Columbia University and the National Institutes of Health / National Institutes of Neurological Disorders and Stroke (NIH/NINDS). It is supported by a five-year grant from NIH/NINDS. The ABC Study is a sub-study of the Norwegian Mother and Child Cohort Study (MoBa), which is a Norwegian population-based pregnancy cohort including about 110,000 children.

Objectives: The scientific aims of the ABC Study are to: (1) establish the Autism Birth Cohort through ascertainment of autism spectrum disorder (ASD) cases from the MoBa cohort, (2) identify environmental factors that may be directly or indirectly associated with ASD, and (3) describe the natural history of clinical, anthropometric and neurobehavioral features of ASD.

Methods: Subjects are recruited into MoBa at week 17-18 of pregnancy. Parents complete questionnaires throughout pregnancy and at intervals following birth (6, 18, 36 months, 7 and 8 years). The data are linked to the Medical Birth Registry of Norway (MBRN). Blood samples are collected from the mother (prenatal and at birth), the father (prenatal) and the child (cord blood at birth). Plasma, DNA and RNA are stored in the MoBa Biobank at -80 degrees C.
Potential ASD cases are identified via three mechanisms: (1) ASD screening of the MoBa cohort in the 36-month questionnaire, (2) referrals by parents or from the healthcare system, and (3) linkage with the Norwegian Patient Registry. The ASD screening is based on the Social Communication Questionnaire (SCQ). There is also a control group of subjects randomly selected from the cohort. Potential cases and controls are invited to a clinical assessment designed to collect detailed neurobehavioral and developmental information and to generate a diagnosis of ASD or associated disorders. The core diagnostic instruments are the ADOS and the ADI-R.

Results: By December 2008, a total of 33,000 MoBa participants have been screened for ASD. Around 500 children have been clinically assessed. All MoBa participants will attain 36 months by mid-2012. Pilot studies of randomly selected Biobank specimens indicate their viability for transcript profiling, proteomics, serology and genetic analyses.

Conclusions: The scientific analyses of the collected data and biological materials have started, with two main focus areas in the initial phase: (1) investigations of potential biomarkers of ASD in child cord blood and (2) child population screening for ASD. Preliminary results will be presented at the conference.

134.97 97 ASD and Autism in the Community. S. Woldoff*[1], L. Blaskey[1], S. Shin[2], J. Pinto-Martin[2] and D. S. Mandell[3], (1)*Children's Hospital of Philadelphia*, (2)*University of Pennsylvania*, (3)*University of Pennsylvania School of Medicine*

Background: Prior studies have found the specificity of autism spectrum disorder (ASD) diagnoses in communities to be high; the methodology of recent prevalence studies is predicated on this assumption. Studies of specificity of diagnosis, however, are more than a decade old. As awareness and community resources for ASD increase, the number of false positives could increase. Understanding the frequency of and factors associated with false positives could help in the interpretation of recent epidemiologic studies and guide strategies to ensure appropriate diagnosis in community settings.
Objectives: To determine whether children placed in autism support classrooms who had received autism support services prior to entering kindergarten also met diagnostic criteria for an ASD using gold-standard evaluation tools.
Methods: The sample included 166 ethnically and economically diverse children in 42 kindergarten-to-second-grade autism support classrooms in one large urban school district. These children received extensive baseline evaluations as part of a larger intervention trial. Evaluations were completed at the beginning of the school year prior to the start of academic programming and included assessment of autism symptoms via direct observation with the Autism Diagnostic Observation Schedule, parent report on the Social Responsiveness Scale, and teacher report on the Pervasive Developmental Disorders Behavior

Inventory. Additional information on adaptive functioning, cognitive development, and use of community services also was obtained.
Results: Preliminary findings suggested that approximately 11% of the sample did not meet current criteria for an ASD on the ADOS. Ongoing analyses are examining factors associated with diagnostic outcome, such as age of diagnosis, participation in early intervention, intensity of interventions, receipt of ancillary services, socioeconomic status, co-occurring medical or developmental problems (e.g., hearing impairment, speech and language delay), and bilingualism.
Conclusions: These findings and their implications for specificity of ASD diagnosis in community samples, as well as factors that may increase a false diagnosis of autism in elementary school age children will be discussed. Possible strategies for future estimation of ASD community prevalence will also be presented. Methodological limitations, including reliance on direct observation versus parent report of symptoms will be considered.

134.98 98 Prevalence of Autism in a Psychiatric Inpatient Population. L. J. Lawer*[1], K. S. Branch[1], E. S. Brodkin[1] and D. S. Mandell[2], (1)*University of Pennsylvania*, (2)*University of Pennsylvania School of Medicine*

Background: Previous studies suggest that autism spectrum disorders (ASD) are over-represented and under-diagnosed in adult psychiatric populations. Adults in state psychiatric hospitals, who received their putative diagnoses prior to the changing conceptualization and increased awareness of ASD, may have undiagnosed ASD. In psychiatrically hospitalized adults, ASD symptoms may appear similar to the negative symptoms of schizophrenia. Four studies have estimated the prevalence of ASD in adult psychiatric populations (inpatient and outpatient) to be between 0.6% and 5.3%; no more than 10% of subjects in these studies who were found to have ASD were previously diagnosed as such. They were most commonly diagnosed with schizophrenia instead.
Objectives: The objective of this study is three-fold: to determine the prevalence of ASD among psychiatric inpatients; evaluate the use of the Social Responsiveness Scale (SRS) as a screening instrument in this sample; and to identify characteristics that discriminate between severely impaired adults with ASD and other psychiatric disorders.
Methods: The sample included 263 civilly-committed patients in one state psychiatric hospital in Pennsylvania. Nursing staff completed the SRS for each patient as part of standard of care. All patients with scores ≥ 100 on the SRS and a stratified random sample of those with lower scores were consented to conduct in-depth chart reviews and contact family members to conduct the Autism Diagnostic Interview-Revised (ADI-R). Chart reviews focused on developmental history, paying particular attention to age of onset and clinical features indicative of ASD. Patients also completed clinical interviews and a neurobehavioral battery to assess the presence and severity of psychotic symptoms and cognitive impairment. Case conferences with two psychiatrists and the team of assessing psychologists will be held for all patients who meet ASD criteria on the ADI-R and a sub-sample of other patients.

Results: Twenty percent of patients received a SRS score ≥100. ADI-R administration and case conferences are ongoing. To date, 31% of those with SRS scores ≥100 met cutoff criteria for ASD on the ADI-R. Based on chart review and clinical observation (including the ADI-R), a third of subjects scoring positive on the ADI-R met criteria for ASD after case conferences (10% of the total sample).

Conclusions: A larger proportion of previously undiagnosed adults in this state psychiatric hospital met criteria for ASD than has been found in previous studies. Previously validated screening and diagnostic instruments, however, including the Social Responsiveness Scale (SRS) and the Autism Diagnostic Interview-Revised (ADI-R), did not demonstrate the same accuracy in this sample as they have in the general population. Improved screening and diagnostic assessments for more severely impaired adults with ASD, especially those that discriminate ASD from other psychiatric disorders, may have important implications for their treatment and supports. The results of this study will aid in efforts to determine the prevalence of ASD among institutionalized adults, increase understanding of the prevalence of ASD in adults, and guide policy and practice regarding diagnostic practices and service delivery to adults with ASD.

134.99 99 Demographics and Diagnosis: Early Findings from the Autism Center of Excellence and Simons Simplex Collection

Studies at UIC. J. Klaver*, M. Huerta, S. J. Guter and E. H. Cook, *University of Illinois at Chicago*

Background: Early recognition and diagnosis of autism spectrum disorders (ASDs) is imperative given the benefits of early intervention. For a particular demographic of children however, there may obstacles to obtaining a warranted diagnosis of an ASD. Though population research has found no differences with regard to the prevalence of ASDs among different ethnicities (Bertrand et al., 2001), work by Mandell and colleagues (2002) found that White children receive a diagnosis of autism an average of 1.4 years earlier than African-American children. What is more, compared to their White counterparts, African-American children are significantly more likely to first receive another diagnosis, such as Attention Deficit/Hyperactivity Disorder (Mandell et al., 2007).

Differences with regard to diagnosis may be even greater as previous studies have restricted their analyses to include only children diagnosed with Autistic Disorder. As such, it is not clear whether population differences exist in the detection and diagnosis of individuals with milder presentations of ASDs. In addition, examining these differences with the use of standardized diagnostic instruments is needed to further our understanding of disparities in diagnosis.

Objectives: This study will examine differences in age of first diagnosis among population groups as well as identify differences in diagnoses assigned prior to the diagnosis of an ASD.

Methods: Subjects will include approximately 120 individuals, ages 3-28 years, participating in genetic studies of autism. Ninety of these subjects identified as White and 30 subjects identified as ethnic minorities. Because of the small number of individuals in ethnic minority categories, these subjects will be collapsed into one category. ASD diagnosis will be confirmed by the use of the Autism Diagnostic Interview-Revised (ADI-R), Autism Diagnostic Observation Schedule (ADOS), and DSM-IV criteria. Analyses will be completed to compare population groups on demographic characteristics and age of first diagnosis. In addition, analyses will examine differences in the diagnoses assigned prior to the ASD diagnosis.

Results: Results of the data analysis described above will be presented. Implications for early identification, diagnostic instrument choice, and clinical education will be discussed. Conclusions: These results will add to our existing knowledge of disparities in the diagnosis of ASDs. Important contributions include the use of gold standard diagnostic instruments and the inclusion of individuals diagnosed with high-functioning ASDs.

134.100 100 Epidemiological Research on Autism in Jamaica: a Preliminary Analysis of Existing Data and Future Research Plans. M. H. Rahbar*[1], M. Samms-Vaughan[2] and K. Brooks[3], (1)*University of Texas Medical School at Houston*, (2)*The University of the West Indies*, (3)*Tropical Metabolism Research Institute*

Background: Autism Spectrum Disorders (ASDs) are complex neurodevelopmental disorders that manifest in early childhood but their etiology is not fully understood. The prevalence of **ASD** appears to be on the rise in developed countries, and has become a serious public health concern. In the developing world, however, reliable epidemiologic data on ASDs are rare. Research in developing countries, where the environment may be very different from developed countries, will broaden epidemiological understanding of autism and allow for a better understanding of the etiology of ASD.

Objectives: The initial goal of this research was to use existing data to characterize ASD in Jamaican children. The long term goal is to develop collaboration among teams at the University of Texas Health Science Center at Houston, Autism Speaks and the University of West Indies in order to build capacity for conducting genetic and epidemiologic research on ASD in Jamaica. We will also present the concept behind the Epidemiological Research on Autism in Jamaica planning project; the first project designed to develop capacity for conducting population-based ASD studies in an Afro-Caribbean population.

Methods: Existing epidemiologic data were of children with ASD who attended the public Child and Family Clinic for Developmental and Behavioral Disorders of Childhood and the only private developmental and behavioral pediatric practice, both at the University Hospital of the West Indies (UHWI); a recognized referral centre for children with ASD. Diagnosis of ASD was based on developmental history, assessment of mental development using the Griffiths Mental Development Scales, and assessment of behavior. Children were evaluated from 1995 through 2006, however standardized assessment and diagnostic procedures for behavior based on

the Childhood Autism Rating Scale (CARS), which is currently used for ASD assessment in Jamaica, was only conducted at both private and public diagnostic facilities for the years since 1999. **Results:** A total of 168 children with ASD were identified during the study period, of which 79 (47%) were seen at the public diagnostic facility. The average age at the first appointment was 4.7 years, the youngest being 1.5 years old and the oldest, 15.8 years old. Of note, 140 (83.3%) were male and the remaining 28 (16.7%) were female representing a 5:1 ratio. Diagnoses were distributed as follows: Autism, 86%, PDD, 6% PDD-NOS, 5%, and Asperger Syndrome, 3%. **Conclusions:** This study provides an important first look at the characteristics of ASD in an Afro-Caribbean population. The reported male-to-female ratio of 5:1 is within range of previous population-based studies (2.8:1–5.5:1). In order to have a better understanding of the etiology of ASD, we will conduct pilot studies to compare ASD case-finding and case-ascertainment approaches that will be used in future studies. Specifically, we will re-evaluate all suspected ASD cases from the existing Jamaica Autism Database using Autism Diagnostic Interview-Revised (ADI-R) and Diagnostic Observation Schedule (ADOS) assessment tools. The agreement between Childhood Autism Rating Scale (CARS) which is currently used for ASD assessment in Jamaica and ADI-R & ADOS will be determined.

134.101 101 Prenatal and Perinatal Risks Factors for Autism in China. X. Zhang[1] and L. Qi*[2], (1)*Tianjin Medical University*, (2)*UC Davis*

Background: Autism is a multifactorial developmental disorder involving both genetic and environmental factors, but the roles of possible environmental risk factors remain unclear.

Objectives: We investigated the effect of prenatal and perinatal risk factors on autism to identify relevant factors in the etiology and the prevention of this disorder.

Methods: A case-control study was conducted using 95 children with autism from six Special Education Schools and two Preschool Autistic Children Special Education Institutions in Tianjin, China, and 95 controls selected by frequency matching on gender and birth year to the cases from regular schools in the same city. Simple and multiple logistic regression models were used to examine the association between autism and risk factors, and to estimate odds ratios and 95% confidence intervals (CI).

Results: Initial unadjusted analyses with simple logistic regression models were used to screen a long list of potential risk factors. This screening identified numerous variables significantly associated with autism ($p<0.05$): 10 maternal and fetal conditions during gestation, including maternal second-hand smoke exposure, mother's emotional state, severe emesis, nuchal cord (umbilical cord wrapped around neck), and 9 characteristics at the time of delivery, such as gestational age < 35 weeks or > 42 weeks, abnormal labor and infant delayed crying. Paternal age (> 30 years old) at delivery and gravidity were also significantly associated with autism. These two factors and the two matching variables (gender and birth year) were used in all multiple logistic regression models and the other potential risk factors were examined one-by-one. After adjusting for gender, birth year, paternal age at delivery and gravidity, all the above 19 significant risk factors remained significantly associated with autism. The following factors had an especially strong association with autism: 1. during pregnancy: maternal unhappy emotional state (OR=3.01, 95% CI: 1.26,7.23, p=0.01), nuchal cord (OR=8.51, CI: 2.70, 26.86, p=0.00), maternal chronic or acute illness (not pregnancy involved) (OR=3.69, 95% CI: 1.30,10.51, p=0.01), maternal second-hand smoke exposure (OR=5.39, 95% CI: 1.72,16.92, p=0.004); 2. at delivery: abnormal gestational age (OR=4.44, 95% CI: 1.71, 11.49, p = 0.002), non-normal labor (OR=2.12, 95% CI: 1.10,4.08, p=0.02) and newborn complication (OR=16.39, 95% CI: 4.78,56.17, p=0.000).

Conclusions: These findings suggest several prenatal and perinatal environmental factors are associated with the risk of autism in children. These specific results may indicate a role for fetal hypoxia, neurotransmitter dysregulation, hormonal, and underlying genetic or chromosomal abnormalities in the etiology of autism.

134.102 102 Can Temperament Add to Our Understanding of Early Autism? Differences Between Toddlers Who Screen Positive for Autism v. Developmental Delay. M. Villalobos*, T. P. Gabrielsen and J. Miller, *University of Utah*

Background: Previous studies have examined the temperament profiles of children with ASD, and increasing evidence is demonstrating it to be a

potentially useful endophenotype in very young children with ASD. Temperament has been demonstrated in the developmental literature to be related to psychobiological traits, which may be implicated early on in children at risk for ASD.

Objectives: The current study compared temperament profiles between toddlers showing significant early signs of autism and toddlers with speech or other developmental delays.

Methods: 817 toddlers born in 2006 were screened at a local pediatric clinic using the M-CHAT and CSBS. Of those who screened positive (after phone follow-up) on the questionnaires, 32 were brought in for an in-person screening with the ADOS, Mullen Scales of Early Learning, and Vineland Adaptive Behavior Scales-II. Seventeen parents also completed the Carey Temperament Scales, before they were told the results of the in-person screening. Seven of these were determined to be showing significant early signs of autism (EA) based on in-person screening measures and clinical judgment. The remaining 8 were determined to be negative for early signs of autism, but had speech or other developmental delays (DD). The EA and DD groups were analyzed for differences in temperament domains (i.e. Approach, Adaptability, Intensity, Mood, Persistence, Distractibility, Threshold, Activity, Rhythmicity). The Mullen Scales were included as a covariate.

Results: A MANCOVA using the Mullen Scales Early Learning Composite (ELC) as a covariate was conducted. The MANCOVA did not indicate a main effect of group (EA versus DD) for the temperament domains ($F(9,4) = .814$, $p = .6$). However, when ELC was covaried the EA group demonstrated a trend toward lower scores on Adaptability (EA: $M = 3.6$, $SD = 1.3$; DD: $M = 4.1$, $SD = .6$; $F(9,1) = 3.5$, $p < .10$) and Approach (EA: $M = 3.3$, $SD = .9$; DD: $M = 4.04$, $SD = .5$; $F(9,1) = 2.6$, $p < .10$).

Conclusions: The present study found that among toddlers who screened positive on the M-CHAT or CSBS-ITC, those who also screened positive by clinical judgment may be more likely to have parental reports of less social approachability toward others, as well as less adaptability, compared to those who screened negative by clinical judgment. This may suggest that temperament characteristics could be helpful in understanding the early presentation of autism, especially from parental reports. Along with social, cognitive, and other domains, this may help us identify early endophenotypes of autism.

134.103 103 Early Signs of Autism Spectrum Disorder in One- and Two-Year-Olds. L. Ruysschaert*, M. Dereu, M. Meirsschaut, G. Pattyn, R. Raymaekers, I. Schietecatte, P. Warreyn and H. Roeyers, *Ghent University*

Background: Early signs of autism spectrum disorder (ASD) are usually studied using retrospective designs. However, these designs are susceptible to several biases, such as selectivity (e.g., in home video fragments) or recall. Therefore, we conducted a large, prospective screening study in Flemish day-care centres.
Objectives: To identify which early signs of ASD are the most common in one- and two-year-olds, and to determine which signs are the most useful in discriminating between infants with and without ASD.
Methods: Personnel of day-care centres received a 3-hour training in recognizing early signs of ASD. Afterwards, child care workers filled out the Checklist for Early Signs of Developmental Disorders (CESDD) for all children. This checklist consists of 25 signs of ASD and was based on a literature review and home video analysis. Children with at least 4 signals were invited for further assessment, including confirming a possible diagnosis of ASD.
Results: The CESDD was filled out for 4036 children between 12 and 36 months of age (mean age = 21.92 months; 51.9% male). Of these children, 85.7% showed no signs of ASD. For 5.8% 1 sign was recognized, for 2.5 % 2 signs were ticked, for 1.4% 3 signs were ticked and for 4.7% 4 or more signs were recognized.
For the one-year-olds (12-24 months), the most commonly indicated signals were: being easily frustrated (4.7%), limited showing (4.3%), and limited declarative pointing (3.5%). A discriminant function analysis revealed that limited declarative pointing, a dislike of being touched or held, and an unusual posture were the items that discriminated the best between children with and without ASD (standardized canonical discriminant function coefficients were .45, .42, and .37, respectively).
For the two-year-olds, the most commonly indicated signals were identical to those of the one-year-olds (6.2%, 4.0% and 3.0%, respectively). The most discriminating items however were different: limited showing, limited response to joint attention, and limited symbolic

play (standardized canonical discriminant function coefficients were .51, .45, and .43, respectively). **Conclusions:** Although being easily frustrated was the most commonly identified signal in both age groups, its discriminative value for ASD was not very high. This indicated that some items on the checklist may be quite common in typically developing children as well. In one-year-olds, limited declarative pointing is the most predictive of a diagnosis of ASD. However, sensorimotor abnormalities (oversensitivity to touch and abnormal postures) also play an important role at this age. In two-year-olds, the most predictive signals are related to joint attention and symbolic play. These results confirm the importance of assessing joint attention and play in young children, but also stress the importance of evaluating non-social factors such as sensorimotor behaviour.

134.104 104 Early Book Sharing Behaviors in An Infant Sibling Study. E. B. Caronna*[1], E. Duursma[2], C. Shieh[1] and H. Tager-Flusberg[3], (1)*Boston Medical Center, Boston University School of Medicine*, (2)*Boston Medical Center, Reach Out and Read National Center*, (3)*Boston University School of Medicine*

Background: The American Academy of Pediatrics (AAP) recommends both routine screening for autism spectrum disorders (ASD) and surveillance for risk factors of ASD from infancy in all children. Parent-child book sharing, widely encouraged by the AAP, provides a potential opportunity to monitor for early signs of risk for ASD. However, no one has yet compared how very young children with and without ASD interact with books. Objectives: 1) To characterize typical behaviors of infants at a very young age (6 to 12 months) while sharing a book with a parent. 2) To identify early signs of atypical development that may herald later ASD and that could be used for developmental surveillance in pediatric clinics. Methods: In an ongoing prospective study of infant siblings of children with ASD and controls aged 6 to 24 months, parents were instructed to videotape themselves playing with their child with a set of toys and books provided by the study. This produced "home video diaries" which were analyzed using a novel coding scheme based on previously developed coding schemata used for analysis of early literacy behaviors and of home videos of children later diagnosed with ASD. Frequency codes measured the following domains: sensory-motor behaviors (physical manipulation or exploration of the book); communication (verbal and/or non-verbal such as vocalizations and gestures); shared affect with caregiver, joint attention; and response to name. Global codes included overall level of parent engagement in book sharing activity, parental affect, and child's affect. Videotapes were coded by two trained coders, and inter-rater reliability was 0.80. Results: Preliminary results are available for 49 families. 60% of the families had at least 1 video diary available, with an average of 4 diaries per family (range: 0 to 21). Most children showed primarily sensory-motor behaviors in relation to the book across all ages analyzed. Verbal communication increased after 12 months of age, with an average of 12 vocalizations per book sharing episode between the ages of 15 to 17 months (compared to 5 or fewer vocalizations before 12 months). Instances of non-verbal communication were rare before the age of 12 months but were more frequent after 14 months (M=1.5, SD=1.77 at 14 months). Joint attention (either initiating or responding to joint attention) was very rare between the ages of 6 to 21 months in the videos analyzed to date. Parental behavior and affect remained stable over time, with most parents showing at least moderate engagement and positive affect. Children's affect was generally neutral in all ages. Conclusions: Observations of parent-child book sharing allow assessment of social interactions and communication in young children. In this preliminary analysis with ongoing data collection, a wide range of behaviors were observed and coded, providing new information about typical and atypical behaviors in young children. When the subjects reach 24 months and are assessed for ASD over the coming months, we hope to identify observable indicators of developmental risk in parent-child book sharing that could be used in pediatric primary care for developmental surveillance.

134.105 105 A Community Screening Program to Detect 1-Year-Old Infants at Risk of Pdd's: Preliminary Results. F. Muratori*, A. Narzisi, S. Calderoni, A. Cesari, C. Grassi, A. Pitanti and R. Tancredi, *University of Pisa – Stella Maris Scientific Institute*

Background: Despite recent studies suggest that autism early signs can be detected in children before their second year of life, only few of them have been performed on large samples of community infants, at their first birthday. In the present study, we used two screening programs, at 12 and 18 months, each of them combining a parent-report instrument with a task the child has been submitted to by the paediatrician.

Objectives: To identify children at risk of PDDs in a community-based sample through the application of the presented screening protocol.

Methods: A preliminary ongoing sample is composed of 180 children recruited in a primary care setting. The first screening program consists in its turn of two different levels. At first level: a) parents fill out First Year Inventory (FYI); b) paediatricians carry out the "response to name" task during medical well-child visits. At second level, children who failed "response to name" and/or met a score above the cut-off in Social-Communication Domain and/or in Sensory-Regulatory Functions Domain and/or in Total score at FYI were evaluated by an expert child psychiatrist with AOSI (Bryson, Zwaigenbaum, McDermott et al., 2007) and ADOS. Chronological (or corrected in preterm) age of 12 months (within the week before or after the baby's first birthday), absence of severe sensory or motor impairments and absence of identified genetic disorders were the inclusion criteria. The second screening program was realized at 18 months of age through a) the filling out by parents of Modified Checklist for Autism in Toddlers (M-CHAT) b) the "joint attention" task administered by paediatrician.

Results: Among the 180 children partecipating in first level screening, 8 were considered at risk (in particular: 3 of them failed both tasks, while the remaining 5 passed the response to name task, but went beyond the fixed cut-off at the FYI). The AOSI and ADOS scales were employed as second level screening instruments on all 8 subjects, in order to reduce false positive. Only one child failed both the instruments and was therefore referred to a diagnostic and therapeutic assessment. The remaining 7 children will undergo a neuropsychiatric evaluation at 15 months of age to monitor chiefly the socio-communicative skills. In order to minimize the false negative results, all the 180 children of the sample will be re-evaluated at 18 months (second screening program) and finally at their third year of life.

Conclusions: This double screening program could be a promising instrument to detect children at risk for PDD, but larger samples are necessary in order to define its most effective use.

134.106 106 Can Early Signs of Autism Spectrum Disorders (ASD) Predict Social-Communicative, Play and General Development in Toddlers with and without ASD?. M. Dereu*, M. Meirsschaut, G. Pattyn, R. Raymaekers, I. Schietecatte, P. Warreyn and H. Roeyers, *Ghent University*

Background: Research has indicated problems in language, cognitive development and social-communicative skills in young children with ASD.

Objectives: To examine if children with early signs of ASD are at risk for developmental and social-communicative problems.

Methods: 39 children who screened positive for ASD in a large screening study in Flemish day-care centres participated in a follow-up study. For these children (61.54% male; mean age = 22.78, SD=6.44) the Checklist for Early Signs of Developmental Disorders (CESDD) was filled out by a child care worker after following a 3-hour training about early signs of ASD. The Early Screening of Autistic Traits Questionnaire (ESAT) was filled out by one of the parents (N=37; 59.46% male; mean age=25.72, SD=7.84). About one year later (mean age=36.17, SD=6.47), the children were invited for further research with the Early Social Communication Scale (ESCS), the Test of Pretend Play (ToPP), the Preschool Imitation and Praxis Scale (PIPS) and the Mullen Scales of Early Learning (MSEL). Of these children, 21 were later diagnosed with ASD (53.8%). Children with and without ASD did not differ on total scores on the CESDD ($t(37)=-0.776$, $p>.05$), on the ESAT ($t(35)=-1.939$, $p>.05$) and on developmental quotient ($t(37)=1.357$, $p>.05$). Children with ASD however, showed less behaviors to initiate joint attention (IJA) than children without ASD ($t(37)=2.349$, $p=0.024$): they made less eye contact with the tester while holding a toy ($t(37)=2.246$, $p=0.031$) and pointed less to objects of interest with coordinated eye contact ($t(37)=2.163$, $p=0.037$). Children with ASD had a lower total score on the PIPS ($t(35)=2.385$, $p=0.028$) but their scores on the ToPP did not differ significantly from children without ASD ($t(34)=1.567$, $p=0.126$).

Results: Because this sample of children with and without ASD did not differ in amount of signs of ASD recognized on early screeners, we studied the predictive power of screening instruments in both groups for later assessment of IJA, imitation, pretend play and general development. Passing or failing items regarding joint attention, imitation and pretend play on the screening instruments, could not predict outcome on the

ESCS, PIPS or ToPP one year later. However, the total scores on the screeners could predict outcome on the MSEL: children with more signs of ASD at T1, had a lower developmental quotient at T2, regardless of their diagnosis (for CESDD: $F(1,35)=5.933$, $p=0.02$; for ESAT: $F(1,33)=7.297$, $p=0.011$). Also, there was a significant interaction effect between diagnosis (ASD or not) and total score on the CESDD in predicting frequency of IJA behaviors at T2 ($F(5,31)=2.451$; $p=0.05$). This effect was mainly due to the frequency of IJA by pointing ($F(1,35)=7.676$; $p=0.009$).

Conclusions: Children with many signs of ASD seem to be at risk for general developmental and IJA problems one year later. The amount of early signs of ASD seems more important for later outcome than the nature of the signs.

134.107 107 Social Visual Engagement in the First Six Months of Life: The Role of Contingency. P. Lewis*, J. B. Northrup, W. Jones and A. Klin, *Yale University School of Medicine*

Background: Typically-developing babies engage preferentially with social aspects of the environment from the first days of life. Examples include both their ability to distinguish adults looking at them from those who are not, as well as their preferential fixation, from at least 3 months of age, to the eyes of other people. An important goal of current research in autism should be to capitalize on these and other early-emerging mechanisms of sociability in order to trace the earliest detectable deviations from normative development. This is a key step in identifying autism at the earliest possible time point. With this goal in mind, recent research in our group has made use of videotaped actresses portraying infant-directed approaches. The videos were created to maximize naturalistic conditions while preserving experimental control. While the utility of these stimuli has been shown, particularly in work with 2-year-olds diagnosed with autism, these stimuli may not be optimal for maximizing between-group differences precisely because they still are not truly natural interactions: videotaped caregivers lack the contingency inherent in real-life, infant-parent interaction. More recently, we developed a testing laboratory that enables live interaction between mother and child, with bi-directional eye-tracking and direct line-of-sight gaze for both parties. In the current proof-of-concept study, we compare visual scanning for typically-developing 1- to 6-month-old infants in two conditions: watching videotaped actresses (Condition 1) and live interaction with mothers (Condition 2). We disambiguate the factors impacting on differences between the two conditions (identity of adult [stranger/mother] versus presence of contingency [videotaped/live]) by adding a third condition: a pre-recorded, and hence, non-contingent, video of the infant's mother (Condition 3).

Objectives: This experiment is intended to test the hypothesis that visual scanning behavior in typically-developing children will evidence discrimination between contingent and non-contingent interactions within the first six months of life.

Methods: Eye-tracking data were collected during each of the three conditions (pre-recorded, live/contingent, and non-contingent). During collection of eye-tracking data, simultaneous video recordings captured the field-of-view of each participant (thus baby's view showed mom, while mom's view showed baby). Field-of-view recordings were coded into four regions (eyes, mouth, body and object) using fully-automated face-tracking and pattern-matching software. The eye-tracking data were then analyzed for time spent fixating on each of the four regions-of-interest.

Results: Preliminary results suggest that typically-developing infants, during contingent interactions with mothers (Condition 2), significantly increase their fixation on eyes as compared with their responses to pre-recorded clips of actresses (Condition 1). Additionally, initial findings show that these children increase their fixation on mouths when viewing non-contingent, pre-recorded clips of their own mothers (Condition 3). These results support our attempts to eliminate a potential confound in the data (lack of contingency, as well as recognition of identity vs. recognition of contingency).

Conclusions: Preliminary results suggest that live interaction increases eye-fixation in typically-developing babies. This experimental paradigm is likely to potentiate between-group differences relative to infants at-risk for autism, thus increasing its utility in the detection of early deviations from the course of normative social visual engagement.

134.108 108 Clinical Characteristics of Children Diagnosed with Autism Spectrum Disorder as Toddlers (<3 yr) vs. as Preschoolers (3-5 yr). L. H. Shulman*, B. M. Burrows, M. R. Galdston, M. D. Valicenti-McDermott, R. Seijo, S. J. Goodman and D. J. Meringolo, *Albert Einstein College of Medicine*

Background:

There is a thrust for earlier identification of children with ASD so that timely intensive therapeutic programs can be initiated. Limited information exists about the clinical profile of children receiving an early diagnosis, with discrepancy in the literature regarding whether children identified earlier have more severe impairment.

Objectives:

To compare the clinical presentation of children diagnosed with ASD before age 3 to children diagnosed after age 3 in a community sample.

Methods:

Retrospective chart review of 323 children, ages 1 to 6, presenting to a University Affiliated Program for multidisciplinary evaluation from 2003 to 2008, who received a diagnosis of ASD. Information reviewed included demographics, medical, developmental, and family histories, DSM-IV symptom checklist, Childhood Autism Rating Scale (CARS), and cognitive level. Statistical analysis included Chi-Square, T-test, Mann-Whitney test, and logistic regression.

Results:

Of the 323, 155 were under 36 months (range 18-72 mo.). Children diagnosed under 3 were more likely to present toe walking (39% vs. 22%, $p = 0.001$) and language regression (22% vs. 13%, $p = 0.04$). There were no significant differences in maternal age or family history of autism. There were no significant differences in autistic symptom severity as assessed by the total CARS score or in cognitive functioning (35% vs. 37% with IQ>70). There were differences in the autistic symptom profile between the 2 groups. On the DSM-IV, children under 3 were more likely to demonstrate lack of showing (61% vs. 33%, $p<0.001$), delay in spoken language (90% vs. 59%, $p<0.001$), and lack of social imitative play (70% vs. 50%, $p = 0.003$). Preschoolers were more likely to present stereotyped language (76% vs. 36%, $p<0.001$), impairment in conversation (48% vs. 13%, $p<0.001$) and failure to develop peer relationships (78% vs. 57%, $p = 0.001$). These differences persisted after adjusting for maternal education, socioeconomic status, and cognitive level.

Conclusions:

Children diagnosed with ASD as toddlers are not more impaired in terms of autistic symptom severity or cognitive impairment when compared to children diagnosed as preschoolers. The children diagnosed earlier are, however, more likely to display toe-walking, and to have a history of regression. Different patterns of autistic symptomatology are also seen in the 2 groups.

134.109 109 Joint Attention in Young Children with Autism. S. Jara*, S. Tek, G. Jaffery, D. Fein and L. Naigles, *University of Connecticut*

Background: Joint attention, which occurs when two individuals focus on the same object or event, plays a critical role in social and language development. Impairment in joint attention is an early sign of autism, and seems to play an important role in later social and language development in individuals with autism. However, previous reports of joint attention (JA) have focused primarily on the number of episodes, on children older than 4 years of age, and on interactions between children and experimenters rather than children and their caregivers. The current report is part of a longitudinal study in which we investigate the JA of young children with autism across a 3-year time span, and relate JA behaviors to concurrent and subsequent language. This report includes data from Visit 1. Objectives: We investigate a variety of joint attention (JA) behaviors of 2-year-old children with autism, during interactions with their parents, and relate these behaviors to other aspects of development. Methods: We tested 10 typically developing toddlers (TYP: mean age = 20.45 months, 7 males), and 10 children with autism (ASD: mean age = 32.32 months, 9 males), who were matched on expressive vocabulary. Children engaged in a 30-minute, structured play session with their parents; these sessions were coded for (a) number of JA episodes, (b) total duration of JA episodes, (c) number of JA episodes which were child-initiated, (d) number of JA episodes that were parent-initiated, and (e) type of toy that was the focus of each JA episode (i.e., toys depicting animates (e.g., dog, baby doll), artifacts (e.g., car, ball), and food and real-life items (e.g.,

snacks, water, bubbles). Joint attention was coded as occurring whenever both child and parent were looking at the same object. Children were also administered the MacArthur Communicative Development Inventories (CDI), ADOS, Vineland Adaptive Behavior Scales (Vineland), and Mullen Scales of Early Learning (Mullen). Results: The ASD and TYP groups did not differ the number and total duration of JA episodes (Ms (ASD) = 28.7 episodes, 16.05 minutes; Ms (TYP) = 35.1 episodes, 17.45 minutes). However, more JA episodes in the ASD group were parent-initiated rather than child-initiated (88.3% vs. 11.6%, $p < .01$); children in the TYP initiated significantly more joint attention episodes than did children in the ASD group (27.7% vs. 11.6%, $p < .01$). The ASD group and the TYP group did not differ from each other in the type of toys they played with during JA episodes. For the ASD group, the number of child-initiated JA episodes was significantly and positively correlated with the CDI, Vineland (all subscales), Mullen Fine Motor, Mullen Receptive and Mullen Expressive scores (ps between .002 - .042). No significant correlations emerged for the TYP group. Conclusions: Number and duration of JA episodes did not vary across groups; however, these 2-year-olds with autism initiated fewer joint attention episodes with their parents. Initiation of JA is related to concurrent social, language, and motor abilities very early in development. Future research will investigate how the JA episodes change across development.

134.110 110 A Comparison of Object Exploration Strategies Between Infant Siblings of Children with Autism and Typically Developing Infants at 6 Months of Age.

A. Bhat*[1], K. Downing[1], J. Galloway[2] and R. Landa[3], (1)*University of Connecticut*, (2)*University of Delaware*, (3)*Kennedy Krieger Institute*

Background:

Infants significantly improve their ability to explore objects multi-modally (i.e. oral, visual, and manual) after the onset of reaching at approximately 5 to 6 months. Between 6 and 12 months, infants will differentially manipulate objects based on properties such as shape, weight, and texture (Ruff, 1984). Infants who later develop autism spectrum disorders (ASD) are known to have fine-motor delays as early as 6 months (Landa and Garrett-Mayer, 2006).

Objectives:

The goal of the present study was to identify object exploration deficits in a cohort of infants at risk for autism (i.e. infant siblings of children with autism (AU sibs)) as compared to typically developing infants at 6 months of age.

Methods:

13 AU sibs and 15 typically developing (TD) Control infants between 6 and 7.5 months of age were observed during an object exploration task. Infants were offered 2 circular (2 inch diameter) and 2 long rattles (4 inch long) that made a noise on shaking. We contrasted long and circular rattles because circular objects require more bimanual coordination for exploration than long objects. The rattle was offered near the infants' hands so that they could easily grasp it without having to reach too far. If the rattle dropped out of their hand, the tester picked it up and offered it again. Infants' exploration behaviors were videotaped and coded later. We coded for duration of grasping with one or both hands and duration of looking and mouthing. In addition, we coded the frequency of transfers from one hand to the other and the frequency of rhythmic arm movements such as shake, bang and rotate. Coders maintained intra-rater reliability of 95% or above for all duration and frequency codes.

Results:

For the circular rattles, AU sibs had significantly shorter grasping durations ($p=0.04$) as compared to Control infants. For long rattles, while there were no group differences in grasping durations; AU sibs had significantly fewer transfers ($p=0.04$) from one hand to another as compared to Control infants. We did not find statistically significant differences for durations of mouthing or looking as well as for the frequency of rhythmic arm movements.

Conclusions: AU sibs had difficulty manipulating objects that required greater bimanual coordination such as circular rattles. They also showed fewer transfers of the long rattle from one hand to another. This further confirmed that AU sibs may have impaired bimanual coordination as compared to Control infants. In contrast, to the past retrospective reports of excessive mouthing in infants who later develop ASD, we did not find significant differences in mouthing durations. However, there were statistical trends for greater looking durations in the AU sibs group. Together, these data suggest that fine-motor deficits in bimanual coordination may be a feature of the broader autism phenotype. Furthermore, these

preliminary results implicate the need for larger studies on fine-motor development of AU sibs. These data also emphasize the need to include object exploration behaviors within early assessment and treatment protocols of ASD.

134.111 111 A Comparison of Reaching Coordination and Arm Postures Between Infant Siblings of Children with Autism and Typically Developing Infants at 3 and 6 Months of Age. A. Bhat*[1], C. Wong[1], J. Galloway[2] and R. Landa[3], (1)*University of Connecticut*, (2)*University of Delaware*, (3)*Kennedy Krieger Institute*

Background: Infants begin to reach for objects between 3 and 5 months of age. In the months before reaching emerges, infants perform a variety of early arm movements that change in a predictable fashion closer to the week of reach onset. The developmental trajectory of transition to reaching is such that infants progress from side to midline postures, closed-handed to open-handed reaches, and accidental contacts to consistent reaching (Savelsbergh and van der Kamp, 1994). Infants who later develop autism spectrum disorders (ASD) are known to have fine-motor delays as early as 6 months. (Landa and Garrett-Mayer, 2006).

Objectives: The objective of this study was to further describe the reaching abilities of infant siblings of children with ASD (AU sibs), a group at higher risk for developing ASD as compared to typically developing (TD) infants at 3 and 6 months of age. We hypothesized that AU sibs would show differences in frequency and quality of reaching as well as duration of specific arm postures as compared to TD infants.
Methods: 15 AU sibs and 15 TD control infants were tested between 3-4.5 months and 6-7.5 months of age. At 3 months, infants laid supine as they attempted to contact a midline toy at arm's length. At 6 months, infants were sitting with minimal support as a toy was presented in the midline and to both sides at arm's length. Video data were later coded for frequency of toy contacts and open-ventral vs. closed-dorsal reaches. We also coded the percent duration of time spent in the following arm postures: at side, on chest, in mouth, in front, and at knees. A single coder maintained intra-rater and inter-rater reliability of above 98%.

Results: At 3 months, AU sibs had significantly fewer toy contacts ($p=0.02$), fewer open-handed reaches ($p=0.009$) as compared to Controls. Analysis of infant arm postures revealed that the majority of the AU sibs placed their arms near the chest or in the front regions without consistent reaching suggesting that AU sibs were either non reachers or emerging reachers. In contrast, the Controls had more experience reaching for objects and the majority of the Controls were consistent reachers. At 6 months, there were no group differences in reaching frequency or quality. However, AU sibs had significantly fewer reach and grasp movements as compared to Controls indicating that AU sibs frequently dropped the toy out of their hand after reaching for it.

Conclusions: The transition to reaching allows infants to independently explore and manipulate their environment. Specifically, object interactions create contexts for communication with caregivers, for learning of object properties, and facilitate future social and cognitive development. Furthermore, fine-motor skills such as reaching and grasping are a foundation for future gestural communication. Thus, our results on delays in reaching and grasping found in AU sibs may be early markers of future non-verbal and verbal communication delays. Overall, these results highlight the importance of incorporating reliable reaching and grasping measures within any early identification tool for ASD.

134.112 112 Joint Attention Revisited: Comparing the Joint Attention Profiles of Young Children with Autism Who Demonstrate Some Joint Attention Ability to MA-Matched Children with DD. S. Hurwitz*, *University of North Carolina at Chapel Hill*

Background: Joint attention (JA) occurs when two people pay attention to the same object or event at the same time and monitor one another's awareness of that focus. JA is an important early communication skill because it is predictive of current language abilities and may be a pivotal skill necessary for future language development. For children with autism, development of JA has been shown to be absent or delayed. Yet there is a subgroup of young children with autism who do employ JA. The types of JA used by this subgroup are unclear, as are the ways in which they compare to children with other developmental delays (DD).
Objectives: This study examined the JA profiles of young children with autism who had the ability to respond to JA. The research questions were: 1) How did children with autism and JA skills compare to MA-matched children with DD with regard to initiating JA, responding to JA, eye contact, gestures, and facial affect used during JA,

and adults toward whom they initiated? 2) Were the children's concurrent language abilities associated with their JA skills and how did they compare across groups?
Methods: A video analysis of JA skills exhibited during taped sections of the ADOS was completed for 40 children. Twenty had autism and were matched on nonverbal mental age (MA) and chronological age (CA) with 20 with DD (M same for both: CA=44mo, MA=26mo). Diagnosis was confirmed by the ADOS and ADI-R. Children were administered the PLS-4 and the Mullen. JA data and language were compared.
Results: Initiating JA—Children with autism initiated JA significantly less frequently than those with DD ($\chi2(1, n=40)=4.434, p<.05$). When they did initiate though, both groups used JA in similar ways: no differences in the frequency with which children used a point, show, or other gesture, if they made eye contact, if they had a positive or negative affect, nor toward whom the bid was directed.
Responding to JA—Children did not differ significantly on the number of JA bids they responded to given the number of bids the adult offered to them ($\chi2(1, n=40)=1.416, p>.05$) but adults did offer more bids to children with autism ($\chi2(1, n=40)=15.17, p<.001$). When responding to JA, children looked very similar, except that those with autism vocalized more than those with DD ($\chi2(1, n=40)=7.46, p<.01$).
The concurrent language scores of the two groups were not significantly different (M=24.1 months autism and M=27.4 months DD); when modeled controlling for MA, diagnosis did not account for language ($F(1)=1.361, p=.251$).
Conclusions: There is a subgroup of children with autism that can use JA in similar ways to children with DD. Though children with autism initiated JA less frequently, when they did use JA (either to initiate or to respond), their JA profiles were very similar to those with DD as were their concurrent language scores. This subgroup of children with autism who have JA may follow a different developmental trajectory, (e.g. may have better concurrent and future language outcomes) than children with autism who do not exhibit JA.

134.113 113 A Quantitative Case Study of An Infant Later Diagnosed with Autism: Response Profiles at 1 and 4 Months. S. J. Sheinkopf*[1], B. M. Lester[1], L. L. LaGasse[1], R. Seifer[2], J. Liu[1], C. R. Bauer[3], S. Shankaran[4], H. Bada[5] and A. Das[6], (1)*The Warren Alpert Medical School of Brown University*, (2)*Warren Alpert Medical School of Brown University*, (3)*University of Miami*, (4)*Wayne State University*, (5)*University of Memphis*, (6)*Research Triangle Institute*

Background: Recent studies, especially those investigating infant siblings of children with autism, have begun to identify signs of autism in the first year of life. These findings suggest that signs of risk for autism are more easily identified after 6 months of age than in the first 6 months of life. Here we utilize a quantitative analysis of an infant later diagnosed with autism as an additional method for investigating this disorder in early development. Objectives: To analyze behavioral responses to a neurobehavioral examination at 1 month of age, and the Face to Face/Still Face procedure (FF/SF) at 4 months in an infant later diagnosed with autism. To compare the infant's responses to a large longitudinal cohort in which this infant was followed. Methods: A male child who is followed as part of the Maternal Lifestyle Study (MLS; a longitudinal study of prenatal cocaine exposure and non-exposed controls) was identified as having Autistic Disorder with moderate Intellectual Disability (child was born premature; GA=28 weeks). Data from the NICU Neurobehavioral Scales (NNNS) at 1-month and the FF/SF at 4 months were analyzed. NNNS data from 454 preterm (<36 weeks) infants were submitted to a latent profile analysis, resulting in four independent clusters, 2 of which consisted of infants with poor neurobehavioral profiles (n= 82 and 42) and poor behavioral outcomes at age 7. The FF/SF included 4 episodes: mother interaction, still face, re-engagement, and examiner interaction. Maternal behaviors, infant positive and negative responses, and degree of match between infant and mother were coded. Percentile scores for the autistic infant were calculated for each variable. Results: On the NNNS at 1 month, the child with autism was classified into the first of the poor NNNS clusters. For the FF/SF at 4-months, infant negative displays were not atypical (between 27th – 40th %iles). Social positive displays were in the upper quartile for the initial play and still face episodes, but in the lower quintile (17th %ile) during maternal re-engagement. Social positive displays were in the upper quintile during the stranger interaction. Notably, the mother was reserved and low in positivity during re-engagement (10th %ile), whereas the examiner was enthusiastically positive. Conclusions: These data indicate that early infant signs of autism may be present, but these results underscore the subtlety of the presentation of autism in the first

year of life. Findings from the NNNS indicated that the autistic child showed nonspecific but poor neurobehavioral responses at 1 month of age. The FF/SF findings were most notable for low positive displays during re-engagement, but – unexpectedly – a high degree of social positive displays during interactions with an exuberant examiner. These findings point to the importance of careful calibration of behavioral protocols to sensitively identify early signs of autism in infancy. These exploratory data also raise the hypothesis that positive behavioral responses may be elicited in infants with later diagnoses of autism, but that these infants may differ in threshold for response.

134.114 114 Gender Differences in Play in Pre-School Autism. C. Holt*, K. Leadbitter, J. Green and .. PACT Consortium, *University of Manchester*

Background: In neurotypical development extensive research has been conducted into sex differences in toy preference and play behaviours (e.g. Maccoby and Jacklin, 1974). Typically girls choose to play with dolls and kitchen toys, whereas boys engage more with cars and construction toys (Jacklin et al, 1984). Girls have also been found to spend more time in pretence play than boys. In autism however, due to the sex differences in the prevalence of the disorder, equivalent studies have rarely been undertaken. Two recent studies, both using parental report, have examined the issue: Case-Smith and Kuhaneck (2008) found that girls with developmental delays (including autism) had a lower preference for doll and figurine play, though this was similarly reduced across the whole sample. Knickmeyer et al (2008) likewise found that girls demonstrated no preference for "female" toys. From parental report, it was also indicated that pretence was preserved to some extent in girls with autism relative to boys.

Objectives: This study extends previous research using a standardised observational methodology. Based on the previous literature we hypothesised 1) that the typical gender preferences found in the literature on neurotypical development would be reduced in girls with autism and 2) girls would demonstrate a relative preservation of play abilities over boys.

Methods: 14 girls and 14 boys (mean age = 44.9 months, SD = 8.2) with autism were individually matched on ADOS module and score. Children were filmed playing with their caregiver for up to 20 minutes with a standardised set of toys. 2 to 12 minutes were coded using Noldus Observer (1991) for toy choice and play behaviours. Participants also took part in the Pre-School Autism Communication Trial (PACT; www.medicine.mancheste r.ac.uk/pact) .

Results: Results indicated that the most popular toy, irrespective of gender, was the garage and cars (mean time of engagement during session = 159s). In addition, girls with autism spent significantly more time playing with dolls ($z = -2.622$, $p = .009$), however marginally engaged with the garage and cars more ($z = -1.992$, $p = .046$). No significant differences were found between girls and boys in their actual play behaviours.

Conclusions: The prediction that girls with autism would show preserved play abilities relative was not supported. The most popular toy choice, regardless of gender, was the garage and cars. Whilst preliminary, these results suggest that typical gender-appropriate play behaviours maybe absent in girls with autism or develop later. A further study is currently underway using the same measures on neurotypical controls matched for non verbal ability and gender. Data from this study will also be available for presentation – and will test whether girls and boys with autism differ significantly from their typically developing counterparts in a contemporary setting.

134.115 115 Improving the Pretend Play Skills of Preschoolers with Autism: The Effects of Video Modelling. E. Boudreau* and B. D'Entremont, *University of New Brunswick*

Background: The development of effective treatment strategies to address the play deficits typically seen in children with autism is of crucial importance. The play activities of children with autism are often repetitive, ritualistic, and lacking in imaginative themes and pretend content. These deficits may contribute to their social isolation by reducing opportunities to engage in interactive play with peers. Video modelling is emerging as a promising intervention technique for improving the play skills of children with autism. This technique involves having the child view a videotaped demonstration of desired behaviour and then providing an opportunity for the child to practice the behaviour.

Objectives: This study examined the efficacy of a video modelling intervention for teaching appropriate play skills to preschoolers diagnosed

with an autism spectrum disorder. Generalization of learned play skills was assessed across settings and stimuli and both short- and long-term maintenance were examined.

Methods: Two four-year-old boys with autism participated. A single-subject design with multiple baselines across subjects was employed. Two videotaped scenarios of an adult playing appropriately with a toy set were created according to the children's ability levels, interests, and intervention goals. Baseline measures of play skills were taken prior to the child viewing the video. Video modelling began after baseline and continued for seven sessions. During video modelling, the child watched the video and was immediately given the opportunity to play with the toy set. There were three additional sessions where the child did not view the video but was reinforced for performing modelled actions and scripted verbalizations. Both children had two generalization sessions, four short-term follow-up sessions, and one long-term maintenance session that took place after a month of discontinuation of all video viewing. Measures of treatment fidelity and social validity were completed.

Results: Both children showed rapid increases in modelled actions and scripted verbalizations during the video modelling phase compared to baseline levels. Generalization and short-term maintenance were achieved for both children. Long-term maintenance was effective for one child only. An interesting increase in unmodelled play behaviours was noted during toy generalization for both children. The unmodelled play behaviours of one child appear to have been suppressed by experimenter-implemented reinforcement of modelled actions and scripted verbalizations. Fidelity measures indicate that the intervention was implemented accurately.

Conclusions: Video modelling was an effective teaching modality for both children. Implications for future research aimed at increasing generalization and unmodelled play behaviours will be discussed.

134.116 116 Enhancing Multidisciplinary Community Supports for Minority Preschool Children with Autistic Spectrum Disorders. V. Nanclares-Nogués*[1], E. Lin[2], C. Rolland[1], M. Cupoli[1] and M. E. Msall[3], (1)*Advocate Illinois Masonic Medical Center*, (2)*University of Chicago*, (3)*University of Chicago Comer Children's Hospital*

Background: Families of preschool minority children with autism often lack access to quality comprehensive interventions.

Objectives: First, to compare communicative and adaptive functional profiles of minority preschool children with autism to other preschool developmental delays and explore the relationships of these measures to parental priorities. Second, to pilot a comprehensive treatment program that is accessible to minority families with limited resources.

Methods: In Phase 1, chart reviews were conducted for 230 children ages 1-3 years with developmental delays in communicative, social-emotional, and adaptive skills. Standardized assessments included Bayley, Capute, Childhood Autism Rating, ADOS, and Vineland Adaptive Behavior Scales. We developed structured interviews for family priorities, indicators of parental physical and mental health, and family supports.

In Phase 2, a 25-hour community-based treatment program known as PUENTES (Spanish word for bridges) for preschool children with autistic spectrum disorders was carried out. Mothers and at least one other family member were intensely trained to implement collaborative interventions to enhance communicative, behavioral, and adaptive skills. Core interventions included, discreet trials, structured teaching, picture exchange communicative systems. Heartland Hand in Hand model, family and sibling supports, speech and occupational therapies, and consultation with educational and human services professionals. Assessments at baseline included Psychoeducational Profile-R (PEP-R), the Adaptive Behavior Scales (VABS), and the Parental Sense of Competence Scale (PSCS). After 4 months, these measures were repeated by raters masked to child's baseline.

Results: Of 230 children in cohort 1, 99 were diagnosed with autism, 83 with mixed developmental disorder (Capute Scale 71-85), and 48 with global developmental delay(Bayley MDI <70). Diagnostic groups differed significantly on communicative and adaptive functioning ($p<0.001$). Children with autism had the most difficulties in communication and adaptive behavior ($p<0.001$). Amongst all groups, parents' initial priorities were getting services (77%) and understanding children's needs (71%). Of the

families seen in follow-up, 60% experienced high levels of stress, and 33% reported high rates of difficulty obtaining supports. Only 50% of parents rated their own physical health as excellent/very good and 22.5% reported peace of mind. Parents rated professionals as most helpful as follows: speech/occupational therapist (94%), physicians (85%), teachers (78%), and school administrators (68%).

Among the children in PUENTES program, major gains in communication, adaptive, and developmental skills occurred. All pre and post changes on PEPS-R, VABS, and PSCS were significant using paired t-tests ($p<0.001$). Parents reported their participation facilitated their children's learning, communication, and adaptive skills and enhanced parental sense of competency. Parents also reported that this collaborative model made them better advocates for comprehensive services that were evidence-based for their children.

Conclusions: Difficulty accessing services and complexity of receiving educational supports are adversely impacting on physical and mental well-being of parents of children with communicative and adaptive functional delays. Our pilot data indicate that a collaborative program that bridges home, school, and the community has the potential to enhance capacity in resource limited settings by providing comprehensive preschool interventions for minority children with autism.

134.117 117 Teaching Symbolic Play in the Classroom to Young Children with Autism. R. W. Saffo* and J. Woods, *Florida State University*

Background: Symbolic play skills represent a core social-communication deficit in young children with autism according to the *Diagnostic and Statistical Manual-IV-Text Revision* (DSM-IV-TR; APA, 2000). For these children, play is developmentally related to two other DSM-IV-TR diagnostic criteria – language and repetitive and stereotyped behaviors (RSB). Recommended practices for early childhood education and special education encourage developmentally appropriate play interventions linking assessment to intervention. Such interventions set in the context of a child's natural classroom environment are lacking, specifically how to integrate these interventions into the preschool curriculum.

Objectives: This study questioned whether teaching young children with autism appropriate play skills within the context of their classrooms would influence their play types, RSB, language skills, and challenging behaviors across time. The researcher hypothesized the children would demonstrate: (a) increased frequency of symbolic play acts on the DPA and increased expressive language from pretest to posttest, (b) increased rates and types of targeted play acts within the intervention that would generalize into the classroom setting, and (c) decreased rates of RSB and challenging behaviors at the onset of intervention that would maintain at lower rates during generalization into the classroom.

Methods: A multiple baseline design across participants was employed. Five preschoolers with autism, aged 44-63 months, enrolled in an early childhood special education (ECSE) program offered by the local school district, participated in this study. Play skills were taught individually through a combined approach of direct and naturalistic instruction within the classroom setting. All sessions were videotaped for later analysis. Observational measures of play types and frequency were based upon the Developmental Play Assessment (Lifter, 2000). Measures of RSB were based upon Watt, Wetherby, Barber, and Morgan (in press). Children's language development was monitored with the Early Communication Indicator (Luze et al., 2001), an IGDI measure.

Results: Children increased their frequency of symbolic play on the DPA and expressive language from pretest to posttest. During baseline, the children's non-symbolic and symbolic play skills remained low and stable. Intervention's onset showed an immediate rise in the target play behavior (non-symbolic or symbolic play) in each child. All children generalized these rates into the classroom and showed maintenance in 1-, 2-, and 4-week follow-up probes. Rates of RSB remained high for all children in baseline. The start of intervention showed an immediate decline in children's rates of RSB that continued across the treatment phase. Challenging behaviors, if present during baseline, showed an immediate decline after the onset of intervention.

Conclusions: This developmentally appropriate play intervention demonstrated the importance and benefits of linking assessment to practice in the natural environment. It revealed a relation

between increased play skills and decreased RSB in the children during intervention that generalized into the classroom setting. Results from this study contribute to interventions supporting functional, social, and communication outcomes for young children with autism in school settings.

134.118 118 Active Engagement in Toddlers Referred for Possible Autism Spectrum Disorder. H. K. Pierce*, A. M. Wetherby, L. B. Swineford and L. Morgan, *Florida State University*

Background: The National Research Council (2001) recommended 25 hours of active engagement (AE) per week of early intervention for children with autism spectrum disorders (ASD). However, there has been a marked absence of research addressing AE for children with ASD. Additionally, there is pressing need for better treatment outcome measures in ASD in light of the priority of early intervention.

Objectives: The purpose of this investigation from the prospective, longitudinal study of the FIRST WORDS Project was to quantify AE in toddlers referred for possible ASD using a new measure of AE.

Methods: Video observations were recorded in the homes of 35 children (17-35 months, *m*=22.5) recruited from the FIRST WORDS Project with red flags of ASD on the CSBS Behavior Sample. Twenty seven received a diagnosis of ASD. Observations were parent-child interactions during 3-5 activities for 40 minutes. Six dimensions of child AE were coded (regulation, productivity, social orientation, eye gaze to face, response to bid for interaction, and communicative act) using 30 second intervals to determine the proportion of AE time. In addition, six dimensions of parent strategies that support AE were measured (promoting participation, routine features, opportunities for communication, balance of turns, synchrony/modeling, and expectations). Measures of nonverbal and verbal development were obtained from the Mullen Scales of Early Learning (17-38 months, *m*=25.2). Adaptive behavior was obtained from the Vineland Adaptive Behavior Scales (17-37 months, *m*=25.7). Measures of autism symptoms were obtained using the ADOS (18-36 months, *m*=26.5).

Results: Young children referred for possible ASD displayed varying levels of AE with regulation occurring at a high proportion of intervals and social orientation and response occurring at low proportions. Significant correlations were observed between regulation and productivity, social orientation and eye gaze, and eye gaze and communicative act. Time samples of varying lengths were not significantly different from one another and were significantly correlated. Forty minute cumulative time samples of response, eye gaze, and communicative act showed significant correlations with outcome measures and added unique variance to predictive models. Although no consistent pattern emerged suggesting that any 10 minute time sample predicted better than the others, 40 minute cumulative samples were the best consistent predictors. Finally, significant correlations were observed between child AE measures and parent support measures.

Conclusions: Measures of AE suggest that regulation and productivity occurred at high proportions in this natural home environment. Social orientation and response to bid occurred at very low proportions suggesting that these may be sensitive measures to detect growth over time. Forty minute intervals were the best consistent predictors of outcome measures suggesting that observations of AE should be a least 40 minutes in length. These findings have important implications for operationalizing AE as a treatment outcome measure of the density of the learning environment for children with ASD.

134.119 119 Assessing Visual Attention in 6-Month-Old Infants with Increased ASD Risk: The Question of Variability. K. M. Venema*[1], E. J. H. Jones[1], A. Gleed[2], M. Elsabbagh[3], M. Johnson[3], A. M. Estes[1], G. Dawson[4] and S. J. Webb[1], (1)*University of Washington*, (2)*Brigham Young University - Idaho*, (3)*Birkbeck, University of London*, (4)*Autism Speaks, UNC Chapel Hill*

Background: Infants who have siblings with an Autism Spectrum Disorder (ASD) are at greater risk for developing ASD than in the general population. Prospective studies of high-risk infants can thus reveal early risk markers for the development of ASD. Previous studies have suggested that poor performance on visual attention tasks may be a risk marker for ASD (e.g. Zwaigenbaum et al., 2005; Elsabbagh et al., 2007). However, little is known about how testing conditions affect this method of assessment. Examining how testing circumstances influence performance on early measures may help us interpret early assessments of infants at risk for

ASD.
Objectives: To examine the influence of testing circumstances on performance on an attention task in infants with and without siblings with ASD.
Methods: Participants were 14 6-month-old infants with siblings with an ASD (sib group) and 13 6-month-old infants with no family history of ASD (control group). In addition to developmental and diagnostic testing, both groups participated in the "gap-overlap" task, where reaction time to shift fixation from a central to a peripheral stimulus was measured. This task involves three trial types: baseline (central stimulus disappears and peripheral stimulus appears simultaneously), gap (central stimulus disappears before peripheral stimulus appears), and overlap (central stimulus remains on screen with peripheral stimulus). Critically, the difference in latency to shift between baseline and overlap trials is thought to reflect the efficiency of attention disengagement.
The task was repeated twice with different stimulus sets. At Visit 1, the task was administered at the end of a lab visit (approximately 90 minutes after arrival); on Visit 2, the task was run at the beginning of the visit.
Results: Replicating previous work, reaction time was slower and more variable on overlap trials than baseline or gap trials in both the control and sib groups. Preliminary analyses indicate that when the gap-overlap task was administered after participation in other tasks, the sib group showed significantly greater difficulty in disengaging than the control group, as observed in a previous study (Elsabbagh et al., 2007). For both groups, there was variability in reaction times between Visit 1 and Visit 2.
Conclusions: Replicating previous work, infants with a sibling with ASD showed slower disengagement than the control group. Inspection of our data raises the possibility that there may be greater variability in the performance of the sib group than the control group across the two testing sessions. Variability in performance may be an important risk marker. Further analysis will increase group sizes to examine whether this finding will hold in a larger sample.

134.120 120 Early Interaction Between Infants with Autism Spectrum Disorder (ASD) and Their Parents: Studies On Expression of Distress. G. Esposito*, P. Venuti and S. deFalco, *University of Trento*

Background: Autism Spectrum Disorder (ASD) is a disorder that affects language and social skills to varying degrees. While many studies have concentrated on examining the patterns of behavior and development in the context of speaking and interacting, very few studies have investigated the specificity of cry in infants with ASD. And this is very peculiar considering that cry can be viewed as both the first communicative system and the first social structure infants can use to communicate with their parents. In our previous studies, waveform analysis showed different patterns in cry episodes of children with ASD and Typically Developing (TD) ones.

Objectives: The aim of this research project is to investigate how the crying of children with ASD, as opposed to TD children and to children with Developmental Delay (DD) is perceived from their parents.

Methods: Different methodologies are being used in this project. In particular, we listed tow studies: (i) Reaction Time experiment for testing whether the atypical structure of autistic cry can bias the parents' perception and (ii) Analysis of Fundamental frequencies of cry.

Results: It has been found consistent agreement among the results of the two studies. All the methodologies showed that cry episodes of ASD seemed to be more similar to those of younger TD or DD children. Balanced for age, ASD cries elicited negative patterns of emotional states as compared to parents' responses to the cries of TD children. These data highlight that cry of children with autism are not well identified.

Conclusions: These results support the view of autism as related to a problem of expressing and sharing emotions. ASD cries have ambiguous patterns, and therefore may not seem understandable. Parents' reactions to autistic cries are qualitatively different from their responses to cries of children with TD of the same age. This difference can be an additional cause of difficulty in sharing feelings and developing inter-subjectivity processes.

134.121 121 Concurrent and Predictive Validity of the MacArthur-Bates Communicative Development Inventory for Children with Autism. V. Smith*[1] and P. Mirenda[2], (1)*University of Alberta*, (2)*University of British Columbia*

Background: The MacArthur-Bates Communicative Development Inventory (CDI) is often used as a measure of early language development for children with autism spectrum

disorders (ASD). However, there is a need for more information on both the concurrent and the predictive validity of the CDI, especially for children who exceed the upper CA limits of the test norms. Objectives: To investigate the relationship between scores on two versions of the CDI (Words & Gestures, WG; and Words & Sentences, WS) and standardized measures of language development in children with ASD. Methods: Participants in Study 1 were 34 children with autism (79% males, mean CA 45 months), whose mean MA on the Mullen Scales of Early Learning was 16.25 months at the first assessment. They were assessed shortly before the onset of early intervention (T1) and an average of 12 and 24 months thereafter (T2-T3), with the CDI:WG, Preschool Language Scale-3 (PLS), Expressive One Word Picture Vocabulary Test, and the Peabody Picture Vocabulary Test-IIIA (PPVT). Spearman rank order correlations were calculated to examine associations between the total number of words understood, words produced, early gestures, and late gestures on the CDI:WG and raw scores on the language measures or subscales thereof, for T1:T1 (concurrent validity) and T1:T2-T3 (predictive validity). Participants in Study 2 were 29 children with autism (86% males, mean CA 61 months), whose mean composite AE on the Vineland was 30.95 months at first assessment. They were assessed 6 months after the initiation of early intervention (T1), and an average of 6 months and 18 months thereafter (T2-T3), using the CDI:WS and the same language measures used in Study 1. Data analysis paralleled that of Study 1, except that CDI:WS subscale scores were used for the total number of words produced, mean words in the child's three longest sentences, and sentence complexity. Results: In Study 1, significant correlations were found between T1 CDI:WG scores for words produced, early gestures, and late gestures and all T1 language measures (r=.34-.60); and between T1 words understood and both PLS receptive language subscale scores and PPVT scores (r=.35-.42). Significant correlations were also found between T1-T2 scores on all CDI:WG subscales except for late gestures and all language measures (r=.38-.69). However, from T1-T3, only words produced and early gestures on the CDI:WG were correlated with all language measures (r=.50-.69). In Study 2, correlations between all T1 CDI:WS scores and all T1 language measures were significant (r=.54-.88). Similarly, there were significant correlations between all CDI:WS scores and all language measures from T1-T2 (r=.51-.73) and from T1-T3 (r=.48-.73). Conclusions: The results provide support for both the concurrent and predictive validity of both the CDI:WG and the CDI:WS for young children with ASD whose chronological ages exceed the test norms. The validity of the CDI for children who are older than the normative group is important information for clinicians in particular, who often experience the limitations of formal tests of language for children with ASD and other significant language impairments.

134.122 122 Triadic Attention Development across Contexts in Infant Siblings of Children with Autism Spectrum Disorders. C. Grantz*, L. Ibanez, W. Gealy and D. S. Messinger, *University of Miami*

Background:
Triadic attention, requesting and sharing interest in events and objects with a social partner, emerges by 12 months of age. It involves infants initiating interactions with a social partner about items in their environment. Children with Autism Spectrum Disorders (ASDs) show deficits in triadic attention. The infant siblings of children with ASDs (ASD-sibs) demonstrate similar, if more subtle, difficulties as their affected siblings, providing a context in which to study the development of triadic attention in an at-risk population during infancy. While much is known about the triadic attention behaviors infants demonstrate with examiners in structured settings, less is known about the behaviors ASD-sibs and typically developing infants demonstrate with their parents in more naturalistic settings.
Objectives:
This study examined the frequency of triadic attention behaviors in ASD-sibs and infant siblings of children without an ASD diagnosis (COMP-sibs) at 8, 10, and 12 months of age across two contexts: A semi-structured setting with an examiner, and a more naturalistic setting with their parent.
Methods:
Two measures of triadic attention were administered to infants at 8, 10, and 12 months of age. During the Early Social Communication Scales (ESCS), a semi-structured measure administered by an examiner, infants were seated on their parent’s lap across the table from an examiner, who presented a variety of stimuli individually. Triadic attention was defined as infants initiating behavioral requesting (IBR) or initiating joint attention (IJA) behaviors. During the Triadic Play Interaction (TPI), a six-minute

naturalistic measure of triadic attention adapted for this study, infants were seated on the floor across from their parent with a variety of toys displayed. IBR and IJA were coded in identical fashion across the ESCS and TPI. For each measure, rate-per-minute scores were calculated by dividing the number of triadic attention behaviors by the length of the measure.
Results:
Preliminary analyses yielded correlations between the rate-per-minute frequency of IJA, $r = .89$, $p < .05$, and IBR, $r = .94$, $p < .02$, across measures at 12 months ($n = 5$ ASD-sibs), suggesting that infants engaging in more triadic attention behaviors on the ESCS also engage in more of these behaviors during the TPI.
Conclusions:
A naturalistic measure of triadic attention with the parent (TPI) at 12 months of age was correlated with a frequently used semi-structured measure of triadic attention with an examiner (ESCS). This suggests that ASD-sibs who demonstrate a high frequency of triadic attention behaviors in one context with an examiner are also demonstrating high levels in a less-structured setting with their parent. This study will continue to examine infant triadic attention behaviors with the addition of 8 and 10 month data and a larger 12 month sample size, in order to better understand the development of triadic attention in ASD-sibs across context and social partner.

134.123 123 Outcomes in Adolescents and Adults with Autism. A. Levy*[1] and A. Perry[2], (1)*York University*, (2)*Thistletown Regional Centre*

Background:

Outcome for adolescents and adults with autism is an important area of research. Studies have examined a number of domains including diagnostic severity, cognitive functioning, language and academic performance, behavioral functioning and social outcomes. The literature suggests that outcomes for this population are highly variable and dependent on factors such as IQ, language development, additional psychopathology and access to services. However, there are a number of limitations to this research. Studies have largely evaluated high-functioning individuals with autism, have examined one aspect of outcome (i.e. cognitive outcome or psychopathology) rather than providing a comprehensive evaluation and have utilized a range of methodologies making comparison of results difficult. These studies have also spanned a wide-time period and, therefore, do not accurately reflect the outcomes for more recent cohorts of individuals with earlier and more comprehensive diagnosis and service provision.

Objectives:

The current study is a retrospective longitudinal study that examines the developmental, psychological and behavioral profiles as well as changes in service utilization in a population of adolescents and adults with autism. The study examined the adolescent's/adult's current level of functioning. The information collected on the individual's cognitive, language and academic level and autism severity rating will be used to create the developmental outcome categories of good, fair or poor. The information gathered on the individual's level of adaptive and maladaptive behavior and service level will be used to create the social outcome categories of good, fair or poor. This information will be coded by two raters and reliability in ratings will be determined. The current study will also examine relevant predictors of the adolescent's/adult's current outcome categories. In order to address this research question, the variables derived from the individual's clinical files, including intake and discharge information, and information from the service interview will be considered as predictors for discriminant functional analysis to predict categorical outcome groups.

Methods:

This study followed a high needs group of adolescents/adults who received comprehensive services through an Ontario specialized intensive tertiary-care program for children and youth with extreme forms of autism. These individuals received a comprehensive evaluation including an assessment of diagnostic severity, cognitive, language and academic functioning, adaptive behavior, social outcomes and comorbid psychopathology. This information was collected using a standard battery of standardized measures that is developmentally appropriate for all participants. In addition, longitudinal data was available on all participants from earlier assessments conducted prior to entering and while in the treatment program. Information on the services and supports these individuals and their families received prior to, during and after exiting the program, was also assessed.

Results:

Preliminary results from 17 participants suggest that the cognitive profile remains stable across time. The majority of individuals made substantial gains in receptive language and domestic skills in programming and maintain these gains at follow-up. In addition, autism symptomatology decreased or remained stable. Further data is being collected and analyzed.

Conclusions:

Initial results suggest that these individuals maintain and continue to acquire skills. Further analyses of developmental profiles, outcomes categories and predictors will be discussed.

134.124 124 Autism Interventions: Making the Evidence Base Accessible. B. A. Fleming*, *Research Autism*

Background: Individuals with autism spectrum disorders, their carers, service providers and others are often confused by the plethora of autism interventions and the claims made for them. This can lead them to try useless, expensive and potentially harmful interventions.

Objectives: The Research Autism website at www.researchautism.net was designed to provide a trusted, objective, scientifically valid and reliable source of information about autism interventions that was also user-friendly and accessible.

Methods: In April 2006 an information manager was recruited to set up and run the Research Autism website. His role included identifying the most commonly-used interventions, researching the claims made for each of these, and identifying any relevant efficacy studies published in peer-reviewed journals. Once a draft had been written up for each intervention, it was sent to a relevant subject expert. That expert checked the information and evaluated each of the peer-reviewed studies using a standardized scoring system. The expert then provided a ranking for that intervention, using a readily-understood system of ticks and crosses. The draft was then sent to a person with ASD, a parent and a service provider to check the user-friendliness of the information. It was also sent to three members of Research Autism's Scientific and Advisory Committee who checked the accuracy of the information and reviewed the ranking provided by the subject expert. Finally, the draft was sent to the full Scientific and Advisory Committee for approval and sign-off.

Results: The Research Autism website now contains information about 100 plus autism interventions. Each intervention is graded according to the level of scientific evidence that has been published in peer-reviewed journals, with links to the abstracts or full papers of relevant studies. The information on the site is available in 10 languages (via Microsoft translator); can be viewed in fonts, sizes and colours to suit the individual, and can be heard via a screen reading system. The site currently attracts approximately 30,000 visitors a month from around the world including individuals with ASD, carers, service providers, researchers and others. The site has had a mixed reaction, with most visitors being extremely positive. For example, Professor Simon Baron-Cohen, Professor of Developmental Psychopathology at the University of Cambridge stated that "The Research Autism website is now the first-choice location internationally if you want to obtain clear, reliable, comprehensive, up-to-date, and independent summaries of the evidence for efficacy of interventions for autism". However there have been some negative reactions from those who support specific therapies, such as facilitated communication, which are not supported by the existing evidence base.

Conclusions: It is possible to create an objective, scientifically valid and reliable resource on autism interventions, which is also user-friendly and accessible to people throughout the world. However there is still a huge amount of work to be done, adding information about more interventions, making the site more user-friendly and accessible, and ensuring that it is promoted to those people who need to know about it most.

134.125 125 Predictors of Daily Living Skills in Children with Autism Spectrum Disorder. L. Gomez*, T. Hutman and M. Sigman, *University of California, Los Angeles*

Background: Children with Autism Spectrum Disorders (ASD) show impairments in daily living skills (DLS) when compared with typically developing children (Liss, Harel, Fein, Allen, et al., 2001). DLS such as dressing, eating, and bathing have implications for children's functional independence and thus for burden of care. Individual differences in DLS are related to IQ in 9-year-old children with low-functioning autism,

but language and verbal memory predicted DLS in higher functioning children (Liss, et al., 2001). Sensori-motor and especially fine motor skills were concurrently related to DLS in preschoolers with ASD (Jasmin, Couture, McKinley, Reid et al., 2008). There is little research exploring predictors of DLS longitudinally.

Objectives: This study sought to determine whether developmental assessments including fine motor and language skills at 12 months predict DLS at 36 months. This study also sought to determine whether predictive relations differed among groups of (1) infants with no family history of autism; (2) infant siblings of children with autism; and (3) infants who received an ASD diagnosis at 36 months.

Methods: Participants included 32 children with no family history of autism and 57 children with at least one older sibling with autism or ASD. 13 of the autism siblings were diagnosed with an ASD by 36 months of age. The Mullen Scales of Early Learning (Mullen, 1995) were administered at 12 months to assess visual receptive skills, fine motor skills, receptive and expressive language. Daily Living Skills were evaluated by parent report using the Vineland Adaptive Behavior Scales (Sparrow, Balla, & Cicchetti, 1984) at 36 months. ASD diagnosis was based on the ADOS-G and confirmed by clinician's judgment at 36 months

Results: Due to variability in baseline measures of DLS, analyses targeted change in DLS from 12 to 36 months. Group membership was associated with change in DLS ($F(2, 76) = 6.60$, $p < 0.01$). The ASD group (M=12.9 months, SD=5.7) made smaller gains in DLS than the unaffected autism sibs (M= 21.7, SD = 7.0) and typical controls (M = 21.4, SD = 8.0). When each of the Mullen Scales was separately entered into a regression model that also included group, the group variable was no longer a significant predictor. Fine motor, visual reception, and expressive language did not predict change in DLS. Only receptive language was a significant predictor of change in DLS, ($\beta = 0.40$, $t(74) = 3.76$, $p < 0.001$) when group was also included in the model.

Conclusions: These findings suggest that variability in receptive language constrains the acquisition of DLS. Children's comprehension of instructions may be an important focus of interventions designed to improve DLS. The longitudinal design of this research may explain the difference in findings relative to concurrent analyses in the research cited above. Longitudinal research contributes significantly to the understanding of individual differences in the acquisition of daily living skills.

134.126 126 Girls. Vs. Boys on the Spectrum. S. Shin*[1], D. S. Mandell[2], S. Woldoff[3] and L. Blaskey[3], (1)*University of Pennsylvania*, (2)*University of Pennsylvania School of Medicine*, (3)*Children's Hospital of Philadelphia*

Background: Research to-date suggests that among children meeting criteria for autism spectrum disorders (ASD), girls are less likely than boys to be diagnosed. Some research indicates that the symptoms of autism in girls generally may be milder, perhaps because social, language and conversation skills develop earlier in girls, ultimately either ameliorating or masking the signs of autism. In addition, evidence from epidemiological and clinical studies shows that the male to female ratio is much higher among those diagnosed with Asperger's or high-functioning autism than it is among those diagnosed with autistic disorder. This may additionally suggest that while girls are diagnosed with autism at a lower rate, perhaps because they present milder symptoms, those that are caught are generally more severely impaired.

Objectives: To examine differences between girls and boys diagnosed with autism in language skill, functioning, and comorbid diagnoses. We hypothesized that girls diagnosed with autism will present with more severe impairments, especially in language and communication skills, and will have more concurrent psychiatric and learning disorders.

Methods: The sample included 160 students enrolled in 39 Kindergarten-2nd grade autism support classrooms in a large, urban school district. Sample demographics closely paralleled district-wide demographics. Subjects were administered the Autism Diagnosis Observation Schedule as a general measure of symptom severity and functional level. Results from the Differential Abilities Scale-II—Early Childhood Core Battery, Bracken School Readiness Assessment—3rd Edition, and Expressive and Receptive One-Word Picture Vocabulary Tests will be used to indicate levels of language skill. Additional information about communication and functional levels will be collected using the Adaptive Behavior Assessment System-II (parent report), PDD Behavior Inventory (parent report),

Child Symptom Inventory-4 (parent report), Aberrant Behavior Checklist (parent report), and Social Responsiveness Scale (parent and teacher reports). In addition, subjects' educational and behavioral health records were reviewed for confirmation of collected data as well as information regarding comorbid diagnoses.

Results: 86% of the sample was male, which is slightly higher than the ratio found in community based studies. Analyses are ongoing. Using results of the ADOS, we will compare the severity of diagnoses between girls and boys. Comparisons of language ability and behavioral and learning disability diagnoses will be made using the results of the assessments and surveys listed above as well as review of their behavioral health and educational records. Conclusions: Results will be used to discuss possible differences in the symptoms and needs of girls and boys diagnosed with autism in early elementary school settings.

134.127 127 The Influence of Culture on Caregiver Response When Completing the Modified Checklist for Autism in Toddlers (M-CHAT). K. B. Oliver*[1], D. L. Robins[1] and A. P. Hazzard[2], (1)*Georgia State University*, (2)*Emory University School of Medicine*

Background:

Autism spectrum disorders (ASD) affect approximately 1 in 150 children in the United States (Centers for Disease Control, 2008). The behavioral expression of ASD symptoms may be associated with behavior phenotypes, which may be expressed differently between ethnic groups (Mandell, & Novak, 2005). Mandell and Novak suggest that parental interpretation of behavior may impact the professional attention given to certain behaviors.

Objectives:

The purpose of this study was to identify items that may be susceptible to cultural biases and misinterpretation. Pediatrician offices in the Metro Atlanta area were invited to participate in the research study. M-CHAT forms were offered to all caregivers at their toddler's 18- and 24-month well-child visit. Completed M-CHATs were scored at Georgia State University, data was entered into a secured data analysis system, and a follow-up interview was used to clarify responses.

Methods:

For this study, M-CHAT scores were compared across children whose ethnicity was reported to be African American or Caucasian. The sample included M-CHAT forms for African American toddlers (n= 682; male= 355, female= 317, no data= 10; mean age= 21 months, *SD*= 3.5, range= 14.9 – 37.5) and Caucasian toddlers (n= 2477; male= 1243, female= 1204, no data= 30; mean age= 20 months, *SD*= 3.1, range= 14.0-49.2). There was no significant difference in age between groups. Maternal education was reported, and found to be significantly different between ethnicities t(2845)= 15.54, p= .000, with the maternal education of Caucasian caregivers being higher. Maternal education was found to be statistically predictive of parental response on 14 of the 23 M-CHAT items; therefore, a binary logistic regression was performed to measure variance attributable unique to ethnicity and not maternal education.

Results:

The results indicated that African American caregivers were significantly more likely than Caucasian caregivers to endorse failing responses on 4 items: plays with toys without mouthing or fiddling them (No), *Odds Ratio (OR)*= 4.497, *p*=.000, *Confidence Interval (CI)*=2.49 – 8.10; makes unusual finger movements near the face (Yes), *OR*=2.465 , *p*=.000, *CI*= 1.92 – 3.15; tries to attract caregiver's attention to own activity (No), *OR*= 1.516, *p*=.041, *CI*= 1.01 – 2.26; sometimes stares or wanders with no purpose (Yes), *OR*= 1.960, *p*= .000, *CI*= 1.50 – 2.55. There were no significant ethnicity differences for toddlers diagnosed with ASD, indicating that the false positive rate appears to be higher in African-American children.

Conclusions:

This study raises attention to specific items on the M-CHAT that may be susceptible to cultural biases or misinterpretation. Results indicate that there may be differences in the interpretation of questions by caregivers based on cultural background, and suggest that some questions operate differently in specific cultural groups. Future research in this area will be important to understand why screening tools may work differently in different ethnic and socioeconomic groups, as usage of screeners becomes more popular and widely dispersed. The follow-up

interview for the M-CHAT, used to clarify item responses, may also need to be revisited with an eye towards providing culturally sensitive clarification for certain items.

134.128 128 The Concurrent Association Between Responsive Maternal Language and Children's Expressive Language Skills Is Moderated by the Specificity of the Mothers' Utterances. M. K. Cornwell*[1], M. J. Sheridan[1], M. Hernandez[1], A. Kemp Ray[1], M. Siller[1], T. Hutman[2] and M. Sigman[2], (1)*Hunter College of the City University of New York*, (2)*University of California, Los Angeles*

Background: Previous research with typically developing children has shown that labeling objects in the child's current focus of attention benefits vocabulary acquisition (Shimpi and Huttenlocher, 2007). Similarly, longitudinal research in autism has shown that undemanding maternal language is associated with children's subsequent language gains (Siller and Sigman, 2002, 2008).

Objectives: This study aims to investigate whether the concurrent relationship between responsive maternal language and the language skills of children with autism is moderated by the presence or absence of specific object labels.

Methods: The sample included 68 children with autism ages 32-82 months (M=57.19 months, SD=12.4 months), with expressive language IQs ranging from 5 - 81.8 (M=29.7, SD=18.5). Children's language skills were assessed using the Mullen Scales of Early Learning (MSEL). Expressive language IQ was calculated by dividing Expressive Language Age by chronological age and multiplying by 100. To collect maternal language samples, mother-child dyads were videotaped for ten minutes with a toy set and given instructions to play as they normally would. A two-minute window of the play interaction was coded for responsiveness of maternal utterances using The Observer® (NOLDUS). The coding system is designed to evaluate two aspects of maternal speech: Demanding vs. Undemanding and General vs. Specific. Demanding utterances are those that aim to elicit a change of behavior from the child, either through correction or overt redirection; Undemanding utterances consist of those that mom uses to describe her own behavior, reinforce or comment upon the child's behavior. In addition, maternal utterances were coded as Specific or General. Specific utterances are those that use nouns to label tangible objects; General utterances use pronouns in the place of noun labels. Utterances were coded as Specific if at least one item was labeled with a noun. Three independent coders established strong inter-observer reliability for all measures (ICC range =.73 to .87).

Results: While demanding specific utterances have no significant association with expressive language (MSEL), r=.047 (p>.05), a significant negative association was found between demanding general utterances and expressive language (MSEL), r= -.401 (p<.01). Conversely, undemanding general utterances have no significant association with expressive language (MSEL), r=.080 (p>.05), but a significant positive association was found between undemanding specific utterances and expressive language (MSEL), r=.354 (p<.01).

Conclusions: These findings suggest that, for children with autism, the association between responsive maternal language and children's expressive language is moderated by the presence or absence of specific object labels. The direction of the relationship between specific object labeling and children's expressive language is unclear; whether children's expressive language skills influence maternal language use, or the other way around, should be the subject of future longitudinal studies.

134.129 129 Who Joins Support Groups for Parents of Children with ASD? the Role of Attitudes and Beliefs. T. Clifford* and P. Minnes, *Queen's University*

Background: Support groups have been shown to be an effective source of support in a number of populations (e.g., Beaudoin & Tao, 2007, Preyde & Ardal, 2003; Singer, et al., 1999). Previous research with parents of children with autism spectrum disorders (ASD) has found that family demographic variables, clinical characteristics of the child, and having been referred by the diagnosing clinician predicted support group use (Mandell & Salzer, 2007). In other populations beliefs and attitudes about support groups have been an important predictor of use (Grande, Myers, & Sutton, 2006; Smith, Gabard, Dale, & Drucker, 1994).

Objectives: This study is part of a larger project examining differences between parents of children with ASD who participate in support groups and those who do not. This study focuses on differences in beliefs and attitudes about support groups.

Methods: Parents of children with ASD were invited to complete a series of online questionnaires measuring their beliefs about support groups and ASD, coping styles, social support, mood, parenting stress, and their child's autistic symptoms and daily functioning.

Results: Data collection is ongoing. We anticipate that parents who participate in support groups will differ from those who do not in their agreement with a number of statements. Specifically, we expect that parents who participate in support groups will be more likely to agree with statements about the usefulness and value of support groups, and will be less likely to agree that support groups are distressing or difficult. We also expect that parents who do not participate in support groups will be more likely to indicate difficulties with the instrumental aspects of attending support groups, such as meeting time, location, and child care.

Conclusions: Learning about the differences between parents who use support groups and those who do not will help in the development of interventions to support all parents of children with ASD.

134.130 130 A Comparison of Mother-Child and Father-Child Interactions during in-Home Play Sessions for Children with Autism. J. H. Elder[1], S. A. Donaldson[1], J. Kairalla[2], R. Bendixen[3], G. Valcante[3], R. Ferdig[3], E. H. Self[1], P. J. Mutch*[4], T. K. Murphy[4], J. Walker[3], C. Palau[1], M. Serrano[1] and T. Galante[3], (1)*College of Nursing*, (2)*Unviersity of Florida*, (3)*University of Florida*, (4)*University of South Florida*

Background: Clinical observations and literature suggest that mothers and fathers interact differently with their children during play. Yet, to date, little data are available evaluating if this is true for children with autism. We have addressed this question in our recently completed analysis of baseline mother-child and father-child play sessions. This is the first report of finalized baseline data analysis from our 4-year NIH-funded study aimed at assisting families in facilitating language development, socialization, and quality family interactions in children with autism.
Objectives: The objective of this initial work was to analyze baseline data and compare social reciprocity behaviors in mother-child and father-child dyads within families. Objectives of our ongoing, nearly completed study of which these baseline data are a part include: (a) to evaluate the effects of training fathers of autistic children with an expanded training module, (b) evaluate the effects of the expanded father training on skill acquisition by mothers, (c) evaluate the effects of the in-home training on parental stress and family cohesion, and (d) develop an Internet-based investigator-father feedback system and evaluate its feasibility during the training protocol and maintenance phases.
Methods: In our clinical work since 1981 and two preliminary studies, we have noted differences in mother-child and father-child interactions. Yet, prior to this current work, observations were not systematically evaluated and quantified. Thus, our first step in analyzing data from our current R01 (2004-2009), was to thoroughly examine baseline data and compare mother-child and father-child social reciprocity behaviors within families during four in-home sessions for 20 mother-child and 20 father-child dyads. Data collection occurred under controlled conditions prior to implementation of the training intervention using videotaping and observational and coding methods that we developed and tested during previous NIH-funded projects. Frequency counts of 2 mother, 2 father, and 2 child behavioral response classes were analyzed using Noldus' Observer program during 10 minutes in-home play sessions.
Results: Mother-child and father-child comparisons of these operationally defined behavioral classes resulted in the following: child initiating ($p=0.278$) child responding ($p=0.306$), parent verbal initiating, including questions directed at the child and verbal directives ($p=0.175$), and parent responding to the child ($p=0.334$). No statistically significant differences were found between any of the mother-child and father-child behavioral data. Further, both mothers and fathers demonstrated low rates of responding (12 and 13) and high rates of verbal directives of 105 and 94, respectively for a 10 minute session. Child initiating and responding mean rates with fathers and mothers were both less than 18.
Conclusions: Results indicating similar behavioral frequencies for mothers and fathers are not consistent with earlier reports of parent differences. Further, high rates of parental verbal directives, low parent responding, and low child initiating and responding rates, suggest the need for more balanced parent child interactions. This second finding lends support for our ongoing and proposed follow up work evaluating a parent intervention designed to promote social reciprocity.

134.131 131 Maternal Influence on the Development of Mastery Motivation in Children with ASD. S. D. Rosenblum*, L. Wainwright and A. S. Carter, *University of Massachusetts Boston*

Background: Mastery motivation (MM) is a young child's drive to explore, persist with, and have mastery over aspects of his/her physical surroundings (Morgan, Harmon, & Maslin-Cole, 1990). The importance of MM lies with its association with later competencies (cognitive and adaptive competence). While young children with autism spectrum disorders (ASD) have been shown to have impaired levels of various forms of motivation (e.g., motivation to explore, learn, and generate actions aimed at a goal) no published studies have examined factors that relate to this impairment. Given the functional impairments of children with ASD in dimensions known to be influenced by early MM, it would be beneficial for both clinicians and researchers to determine external factors that may influence MM. Maternal behaviors represent a group of external factors that may serve this role. Research regarding maternal influence on children with ASD is a delicate endeavor, due to early research suggesting a causal link between maternal behavior and the symptoms of autism. While this accusation is now universally unsupported, researchers have remained hesitant to examine the effect mothers may have on their child with ASD. However, recent empirical studies have begun to examine the beneficial effects that caregivers' behaviors may have for children with ASD (Doussard-Roosevelt et al., 2003). Among non-ASD children there is evidence that maternal sensitivity and maternal cognitive engagement may be positively related to MM development (Hauser-Cram, 1996; Gaiter et al., 1982). Further, among children with ASD, maternal cognitive engagement, maternal sensitivity, and low levels of maternal intrusiveness have been shown to be positively related to other areas of development.

Objectives: This study aims to determine whether maternal cognitive engagement, maternal sensitivity, and maternal intrusiveness are related to the development of MM in children with ASD.

Methods: The study included 80 children, age 18 – 33 months, diagnosed with ASD. All children met criteria for an ASD based on the ADI and the ADOS, as well as an expert's clinical impression. Two measurements of MM were collected, based upon the child's behavior observed by trained coders (MMO) and parental report (MMP). Maternal influence was assessed by trained coders viewing a seven-minute play interaction between a mother and her child, during which they were provided with toys and the mother was asked to play with her child as she normally would. The Parent-Child Interaction Rating Scales (Sosinsky, Carter & Marakovitz, 2004) were used to assess Maternal Cognitive Engagement level, Maternal Sensitivity level, and Maternal Intrusiveness level.

Results: Data have been collected and results are pending analyses. Hierarchical regression will be used to examine the direction, strength, and significance of the relationship that exists between maternal characteristics and MM (both MMO and MMP). It is hypothesized that when controlling for the child's developmental quotient (DQ), symptom level, and age, Maternal Cognitive Engagement and Maternal Sensitivity will be positively related to a child's MM. Finally, when controlling for DQ, symptom level, and age, Maternal Intrusiveness will have an inverted U-shaped relationship with child's MM.

Conclusions: Conclusions are pending analyses.

134.132 132 The Experience of Maternal and Family Care for Autism Over the Course of Pediatric Development. D. B. Nicholas*[1], P. McKeever[2], L. Zwaigenbaum[3], R. MacCulloch[4] and W. Roberts[5], (1)*University of Calgary*, (2)*Bloorview Kids Rehab and Hospital for Sick Children/ University of Toronto*, (3)*University of Alberta*, (4)*The Hospital for Sick Children*, (5)*University of Toronto*

Background: Autism is a developmental disorder that affects children's personal, familial, scholastic, and community experiences and relationships. Intensive ongoing home-based treatment is needed by many children with autism. Research identifies mothers as these children's primary caregiver, and as central in accessing, navigating and, in many cases, providing needed resources and treatments. Despite mothers' integral role, there is a dearth of research addressing these roles, and the experiences and needs of mothers and their families over the extended course of this caregiving journey. Understanding this shifting nature of care, including maternal and family needs, is crucial in ascertaining challenges, gaps and areas for intervention.

Objectives: The purpose of this study is to evaluate this shifting nature of maternal and

family care of children with autism over the course of child and adolescent development. The study will ultimately serve to identify needs for home- and community-based care.

Methods: This study draws upon a mixed-method qualitative design. Data collection comprises three phases: (1) semi-structured interviews with caregiving mothers at varying points in their child's development (diagnosis, pre-school, elementary school, junior high, high school, transition to adulthood), (2) participant observation in the homes of families at diverse developmental ages/stages (including follow-up family interviews), and (3) a Delphi consultation identifying guiding statements and recommendations for practice and policy advancement.

Results: Findings from Phase 1 qualitative interviews will be presented. Findings will address the roles, experiences, strengths and challenges of mothers and families who are caring for a child with autism. Greater knowledge about these important realities will ultimately lead to increased awareness of maternal needs, with the potential for increased targeting of services to meet needs. By identifying the needs of caregiving mothers over time, the quality of life and sustainability of these mothers and their families, have the potential to be supported. Given the demanding and shifting challenges of autism-based maternal care, upholding and supporting mothers, as key caregivers, is of paramount importance.

Conclusions: Current gaps in understanding maternal experiences over time, will be redressed by illuminating the temporal shifts of maternal care for children with autism. Based on emergent findings, future priorities for further family-based autism research, including potential intervention studies, are expected.

134.133 133 The Effects of Parental Stress on the Emergence and Development of Joint Attention Behaviors in Infant Siblings of Children with Autism. J. Johnson*, E. A. Koterba, M. V. Parladé and J. M. Iverson, *University of Pittsburgh*

Background: Younger siblings of children with autism (Sibs), themselves at heightened biological risk for autism, are also susceptible to developing social, emotional, and communicative difficulties (e.g., Yirmiya et al., 2006). Parent stress levels, already enhanced due to having an older child with ASD (Fishman et al., 1989), may influence parent/infant interaction and subsequent development of infant joint attention skills (Siller et al., 2002). However, the potential impact of parental stress on younger siblings' development has yet to be examined.

Objectives: The goals of this study were to: (1) describe the development of joint attention behaviors in Sibs from 12 to 14 months; and (2) identify potential relationships between parental stress and infant joint attention.

Methods: Eighteen infant siblings of older children previously diagnosed with autism (9 males) were videotaped at 12- and 14- months during administration of the Early Social Communication Scales (ESCS; Mundy et al., 1996) by a trained experimenter. The ESCS is a semi-structured assessment of children's nonverbal communication skills and yields a measure of higher level initiating joint attention (IJA) involving eye contact coupled with a conventional gesture (i.e., showing or pointing). At 12 months, primary caregivers completed the Parenting Stress Index (PSI; Abidin, 1983), to assess the level and source of parental stress. Two subscales from the PSI that specifically assess parent/infant interaction were examined here: Reinforces Parent (RE) and Attachment (AT). Based on responses from these subscales, infants were classified as having a caregiver who reported: (a) high stress levels on both subscales (HS-sibs); (b) low stress levels on both subscales (LS-sibs); or (c) mixed stress levels (high scores on one subscale; MS-sibs). Because lower scores on these subscales are suggestive of a stronger parent/infant relationship (Abidin, 1983), LS-sibs were expected to exhibit more IJA bids at 12 and 14 months and the greatest increase in IJA bids across sessions.

Results: Preliminary analyses indicated that at 12 months, IJA behaviors were relatively infrequent in all three groups ($Mdn_{\text{LS-sibs}} = 0.00$; $Mdn_{\text{MS-sibs}} = 1.50$; $Mdn_{\text{HS-sibs}} = 0.00$). Counter to our prediction, HS-sibs exhibited the greatest increase in IJA behaviors from 12 to 14 months and produced roughly three times as many IJA bids as LS- and MS- sibs at the 14-month session ($Mdn_{\text{LS-sibs}} = .667$; $Mdn_{\text{MS-sibs}} = 1.00$; $\text{Mdn}_{\text{HS-sibs}} = 3.00$). Furthermore, there were significant positive correlations between 14 month IJA frequency and parent stress levels on both the RE subscale, $\rho = .665$, $p = .036$, and the AT subscale, $\rho = .660$, $p = .038$.

Conclusions: Together with other research demonstrating variability in IJA skills among Sibs (e.g., Goldberg et al., 2005) these findings suggest that familial factors such as parent/infant

interaction patterns may buffer against risk for early communicative delay to produce more positive outcomes. Increased anxiety may serve as a motivating factor for some parents, who may become more active in engaging their child in interactions that support the development of IJA skills, an effect that may be particularly beneficial for at-risk infants.

134.134 134 High-Atypicality Autism Siblings: a Prospective Study of Mother-Infant Interactions. M. W. Wan*[1], J. Green[1], M. Elsabbagh[2] and M. Johnson[2], (1)*University of Manchester*, (2)*Birkbeck, University of London*

Background: Infant siblings of children with autism spectrum disorder (A-sibs) –who are themselves at genetic risk of autism –are more likely to exhibit early social and communicative impairments than typically developing siblings (TD-sibs). Recent prospective observational studies, including our own, further found that mother-infant interactions in A-sibs show specific subtle but consistent impairments in early-middle infancy, which may exacerbate the infants' social atypicalities through their experiencing or seeking of a less optimal early interactive environment. Little is known about the developmental trajectory of such mother-infant interactions through the first year.

Objectives: To compare mother-infant interaction characteristics: (1) between A-sib infants with and without high phenotypic autism risk, and TD-sib controls in a follow-up at 12-15 months; (2) within groups to investigate longitudinal consistency between 6-10 months and 12-15 months.

Methods: Fifty-five mother-infant unstructured play interactions were rated, blind to dyad information, using a global rating scale on which we have previously reported validation and reliability data, and adapted for a slightly older age group. Infants were 12- to 15-month-old A-sibs at high phenotypic risk (i.e. top quartile scores on an independent standardised measure of autism phenotype behaviour) and low phenotypic risk, and TD-sib controls.

Results: We previously reported that A-sib infants with high phenotypic atypicality at 6-10 months were more likely to exhibit mildly avoidant interactive behaviour, and – as a group – their mothers were significantly less sensitive and less accepting of their infant's behaviour. Here, we attempt to replicate in the same sample these findings at 12-15 months, and will report whether such interactive impairments could be predicted by interactions or phenotypic atypicality at 6-10 months. We will also present findings at both time points after controlling for infant temperament and IQ.

Conclusions: This study was the first to show prospectively that A-sib infants at high phenotypic risk *and* their mothers tend to exhibit interactive impairments at 6-10 months. The stability or exacerbation of such impairments in middle infancy would have clear implications for prodromal intervention.

134.135 135 Parents' Perspectives on Community-Based Mental Health Services for Children with Autism Spectrum Disorders. L. I. Brookman-Frazee*, *University of California, San Diego*

Background: Children with autism spectrum disorders may be served in community-based mental health settings for behavioral and psychiatric problems commonly associated with ASDs. In California, these mental health services may be linked to the educational system for students for whom emotional and behavior problems interfere with their academic functioning (through funding established with state legislation). Little is known, however, about families' experiences accessing mental health services or their perceptions of the impact of care. Understanding families' experiences is critical to efforts to improve community-based services.

Objectives: To gain an understanding of families' experiences with mental health services.

Methods: Qualitative data regarding families' experiences with mental health services were collected as part of a larger study aimed to understand the clinical characteristics of children with ASDs served in these settings and the training needs of the providers who serve them. Twenty-one semi-structured interviews were conducted with parents of children with an ASD who were currently receiving or had previously received mental health services in San Diego, CA. Parents were asked about the characteristics of their children, their service use histories, barriers to accessing mental health care, and their perceptions of the impact of mental health care. The interviews were transcribed and analyzed for a priori and emergent themes.

Results: The analyses revealed a number of themes related to families' experiences within the

mental health system and the interactions between the mental health and education systems. Most of the children involved in the mental health system were high functioning and diagnostically complex (i.e., had a history of diagnostic uncertainty and multiple diagnoses) and were referred for treatment for externalizing behaviors. Access to mental health services was often facilitated by and funded through the educational system following severe behavioral escalation and linked to the child's individualized education plan. Although some parents felt that weekly outpatient therapy, specifically, provided important emotional support to their child, many expressed frustration by the minimal impact of these services. The limited number of mental health providers with specialized ASD training was viewed as a significant barrier to accessing effective care. Navigating the mental health and educational service systems and interactions with mental health providers and educators were viewed as significant sources of stress to many families.

Conclusions: These data have important implications for efforts to improve services for children with ASDs. Results suggest that efforts are needed to further examine the interaction and coordination between service systems, paying particular attention to the role of the educational system in facilitating mental health services. Further, these data also suggest that efforts to build capacity in the mental health system to effectively serve this population are clearly needed. Lastly, the results underscore the importance of the added stress that interactions with professionals and navigating services can have on families. The implications of these findings for developing a clinical training model for providers within the mental health system will be discussed.

134.136 136 Feeding a Child with Autism Spectrum Disorder: Mothers' Strategies and Beliefs. L. G. Rogers*, J. Magill-Evans, G. Rempel and L. Zwaigenbaum, *University of Alberta*

Background:

From the moment of their child's birth, mothers commence the intricate dance of responding to their child in order to meet his or her feeding needs. This can be particularly challenging when the child has Autism Spectrum Disorder (ASD) as 46-89% of children with ASD have feeding challenges (Ledford & Gast, 2006). The frequency of feeding challenges is greater than in typically-developing peers (Schreck, Williams, & Smith, 2004). While the descriptive studies have provided information on the types of feeding challenges for children with ASD, there is no research investigating how feeding challenges develop, change over time, and what mothers do to ensure that their children with ASD have adequate nutrition.

Objectives: The research questions are: For mothers, what is the process of feeding their children with ASD from infancy to school age? What challenges do the mothers face? What strategies have been used? How successful were these strategies?

Methods: This study used a constructivist grounded theory approach. Grounded theory is the method of choice when pursuing a question that is process oriented, when there is change over time, and the research purpose is to identify social processes (Richards & Morse, 2007). Participants were eight mothers of children aged five to nine years with a confirmed diagnosis of ASD and feeding challenges. Mothers whose children had a co-morbid diagnosis that could independently affect feeding were excluded from the study. Interactive interviews in the family home were recorded, transcribed and analyzed (Charmaz, 2006). Field notes were recorded following each interview. The goal is to develop theory for clinical practice through the analysis of the data. Appropriate ethics approval was obtained.

Results:

Results are presented as themes derived from the interview and field note observational data. Themes including parental belief systems and family values, mothers' roles, stress around feeding, impact on family and extended family, and strategies mothers use are reported along with supporting quotes. Strategies ranged from common approaches such as gradually and persistently offering new foods to novel approaches such as presenting new foods at a restaurant buffet. Parental beliefs and values influenced and shaped the strategies used by mothers, for example the value placed on calm family mealtimes or the belief that food choices influenced their child's behaviours.

Conclusions:

There are few studies specifically investigating ASD and feeding challenges. Findings from this study will help to determine appropriate areas for foci in assessment and appropriate treatment interventions. There is evidence to suggest that health care professionals need to consider the cognitive, affective and behavioural domains of family functioning (Wright & Leahey, 2005) when devising interventions to address difficulties within the feeding process. Preliminary data analysis suggests there is no standardized intervention for feeding difficulties and an individualized approach needs to be based on the child's needs and the family's beliefs and values and offered within a trusting, mutually respectful parent-professional relationship. This study will be of interest to those interested in understanding the experiences of families living with the challenges of ASD in order to more appropriately support them.

134.137 137 Predictors of Insightfulness in Mothers of Children with Autism. S. L. Marshall*[1], T. Hutman[1], M. Siller[2] and M. Sigman[1], (1)*University of California, Los Angeles*, (2)*Hunter College of the City University of New York*

Background: Maternal insightfulness is a mother's ability to consider a child's thoughts and feelings and to relate that information to the child's behavior while discussing actual mother-child interactions. Insightfulness has been linked to mothers' synchronous behavior during play with children with autism (Hutman, Siller, & Sigman, in review). Maternal insightfulness has also been linked with sensitive caregiving behavior and children's quality of attachment in a non-clinical population (Koren-Karie, Oppenheim, Dolev, Sher, et al., 2002). In mothers of children with autism, insightfulness was not related to the child's chronological age, language or non-verbal IQ. Furthermore, classification on the Insightfulness Assessment was not related to mothers' age, ethnicity, years of education, or household income (Hutman, Siller, & Sigman, in review).

Objectives: To enrich current understanding of insightfulness in mothers of children with autism and to explore links with other maternal social cognitions including perceptions of stress, social support, gratification and efficacy in parenting. We hypothesized that Positively Insightful mothers would report less stress, more social support, more gratification and efficacy from parenting than non-insightful (One-Sided and Disengaged) mothers.

Methods: Participants were biological mothers of sixty-seven children with autism under the age of seven. Autism diagnoses were confirmed, cognitive and language development were assessed, and mother-child interactions were filmed during two visits to our research lab. Two-minute video clips from these interactions were the basis of the Insightfulness Assessment (Koren-Karie & Oppenheim, 1997), which was conducted in families' homes an average of 19 days after the second lab visit. The following social cognition questionnaires were completed after the interview had been conducted: Clarke modification of Holroyd's Questionnaire on Resources and Stress (QRS-Clarke; Konstantareous et al., 1992); the Perceived Social Support from Family Scale (Procidano & Heller, 1983); the Parenting Sense of Competence Scale (Gibaud-Wallston & Wandersman, 1978).

Results: Hypotheses were tested with one-tailed t-tests. Positively Insightful mothers (n = 23; 34.3%) reported less stress overall than One-Sided mothers (n = 21; 31.3%), with differences in the domains of family sharing; sacrifice; time demands; and family enrichment. Positively Insightful mothers reported higher levels of efficacy than One-Sided mothers. Positively Insightful mothers perceived higher levels of social support than Disengaged mothers (n = 23; 34.3%). P values were less than 0.05.

Conclusions: Individual differences in mothers' responses to the Insightfulness Assessment are associated with measures of perceived stress, efficacy, and social support. Mothers whose narratives about their child with autism were classified as Positively Insightful report less stress, more efficacy in the parenting role, and more support from family than non-insightful mothers. These findings suggest targets for interventions that aim to enhance mothers' ability to take their child's perspective, a skill that has been associated with improved language development in children with autism (Siller & Sigman, 2002; 2008).

134.138 138 Sleep and Behavior in Children with Autism Spectrum Disorders-Effects of Supplemental Melatonin. K. Adkins*[1], S. G. McGrew[2], W. Stone[1], K. L. Surdyka[1], S. E. Goldman[1], D. Wofford[1] and B. A. Malow[1], (1)*Vanderbilt University*, (2)*Monroe Carell Children's Hospital at vanderbilt*

Background:

Children with autism spectrum disorders (ASD) have lower levels of melatonin and melatonin metabolites than typically developing children. Retrospective and small open label studies have shown that melatonin promotes sleep in children with ASD, with excellent tolerability and minimal adverse effects.

Objectives:

We are performing a prospective dose-response trial of supplemental melatonin in children with ASD. Our objectives are: (1) To identify optimal dose, tolerability, and adverse effects and (2) To study the impact of supplemental melatonin on sleep and daytime behavior.

Methods:

We included children ages 4-10 years with a clinical diagnosis of ASD, confirmed by the Autism Diagnostic Observation Schedule and Autism Diagnostic Interview-Revised, who took 30 minutes or longer to fall asleep on 3 out of 7 nights per week. Parents completed sleep and behavioral survey forms at the beginning and again at the conclusion of all study procedures. Behavioral measures included the Children's Sleep Habits Questionnaire (CSHQ), the Repetitive Behavior Scale (RBS), and the Parent Interview for Autism-Clinical Version (PIA-CV). Children wore actigraphy watches (Mini Mitter, Respironics) for 17 weeks to provide an objective measure of sleep latency (time to fall asleep).

After one week of baseline actigraphy was recorded, parents were instructed to give their child inert flavored liquid for two weeks, 30 minutes before bedtime, to acclimate the child to taking a medication at bedtime. Once the acclimation period was completed, melatonin (Natrol ®) dosing was begun at 1 mg. The dose of melatonin was escalated every three weeks, to 3mg, 6mg, and 9 mg, until the child achieved a "satisfactory response," documented by actigraphy, defined as falling asleep within 30 minutes of bedtime on 5 out of 7 nights per week. The first three weeks and last three weeks of actigraphy were combined in each child to produce a baseline and treatment sleep latency. Baseline and treatment measures were compared using a Wilcoxon signed-ranks test.

Results: To date, 10 children have completed the study. All children tolerated melatonin with no adverse effects. Nine of 10 children tolerated actigraphy and achieved a satisfactory response at relatively low doses—3 children at 1 mg and 5 children at 3 mg with only 2 children requiring 6 mg and none requiring 9 mg. Sleep latency decreased from 38.7 ± 22.5 minutes (mean ± standard deviation) to 21.8 ± 7.9 minutes ($p = 0.039$) with treatment. Improvements with treatment were also noted in CSHQ domains of sleep onset delay ($p = 0.008$) and sleep duration ($p = 0.004$), RBS domains of compulsive ($p = 0.002$) and ritualistic ($p = 0.004$) behavior, and the PIA-CV domain of affective responses ($p = 0.02$). One child did not respond to melatonin by parent reports and surveys, and did not tolerate actigraphy. She was later diagnosed with bipolar disorder and treated with risperidone, with improved sleep.

Conclusions:

Low-dose supplemental melatonin is a well-tolerated treatment for insomnia in children with ASD, and appears to impact favorably on both sleep and daytime behavior. Randomized clinical trials appear warranted.

134.491 91 Prevalence Rates of PDD among Children at the English Montreal School Board. T. Lazoff[1], T. Piperni[2], E. Clarke[2], L. Lewis[2] and E. Fombonne*[3], (1)*Montreal Children's Hospital*, (2)*English Montreal School Board*, (3)*McGill University*

Background:

In recent years, studies have revealed an increase in prevalence rates of Autism and other Pervasive Developmental Disorders (PDD). The causes for such increases are not entirely understood, but may reflect factors such as study methodology, improved methods of detection and widening of diagnostic criteria.

Objectives:

To determine prevalence rates of Autism and other PDD among Anglophone, school-aged children in Montreal, Quebec.

Methods:

23,664 children aged 4 to 17 years old were surveyed from the English Montreal School Board (EMSB). All the data was obtained from educational records and therefore, no direct examination of any children was required for this

research. Children with a diagnosis of a PDD at the EMSB are assigned a special education code of 50. The special education codes are finalized by the end of March each year, and therefore, we selected a survey date of April 1, 2008. For all children with a diagnosis of PDD, information was obtained about their diagnostic subtype, age of diagnosis, current age, gender, current grade, the location of their diagnosis and the school they were attending. Prevalence rates were then calculated.

Results:

Out of a population of 23,664 children enrolled in the 71 schools of the EMSB, a total of 206 were identified by a special education code of 50 with a diagnosis of a PDD. The prevalence for all PDD was 8.71/1,000 (95% CI: 7.56 - 9.96 /1,000). For PDD specific diagnoses, the prevalence was 2.87/1,000 (95% CI: 2.23 - 3.64/1,000) for Autistic Disorder, 4.61/1,000 (95% CI: 3.78-5.55/1,000) for PDD-NOS, 1.18/1,000 (95% CI: 0.79 - 1.71/1,000) for Asperger Disorder, and 0.04/1,000 (95% CI: 0.00 - 0.24/1,000) for Childhood Disintegrative Disorder. There was a significant linear increase in birth cohort prevalence proportions from older (Grade 11) to younger (Kindergarten) birth cohorts. In the sample, there were 174 males and 32 females resulting in a 5 to 1 male to female ratio. Of the 206 children with PDD, 16 attended a special needs school and 190 attended a regular school. Of the 190 attending a regular school, 16 were placed in segregated classrooms, while 174 were placed in integrated classrooms. Of the 174 attending integrated classrooms, 165 were assigned a child-care worker and 9 did not have any child-care worker to facilitate their integration.

Conclusions:

This study provided additional evidence that the prevalence rate of ASD is close to 1%, as per several recently published surveys. Recent birth cohorts yielded significantly higher rates than older ones. The reasons for this trend could not be examined with our methods.

Invited Educational Symposium Program
135 Menage A Trois: Immune System, Brain and Behavior – Relationships Between the Three

Speakers: R. S. Fujinami[1]B. T. Volpe[2]M. W. Cunningham[3]D. G. Amaral[4](1)*University of Utah School of Medicine*, (2)*Weill Medical College of Cornell University - Burke Institute*, (3)*University of Oklahoma Health Sciences Center*, (4)*University of California, Davis*

Immune responses to central nervous system (CNS) components have been considered as a potential factor in the development of autism. This session will provide a contextual basis for the immune response, i.e., provide an overview of the immune system and how immune responses to CNS components can arise. Speakers will present several systems where immune responses to CNS antigens lead to alterations in behavior. The first speaker Dr. Robert Fujinami will present an overview of the immune system and some of the mechanisms that can generate immune responses to the CNS. Dr. Bruce Volpe will describe a subset of patients with systemic lupus. These patients have antibodies to DNA which cross-react with subunits of the NMDA receptor. These antibodies are found in the cerebrospinal fluid of the patients and correlate with impaired brain function. Dr. Madeleine Cunningham will present data describing immune reactivity in Sydenham's chorea patients to particular proteins found on the surface of neurons. These antibodies cross-react with the Group A Streptococcus and affect neuronal function. The antibodies correlate with CNS manifestations in patients with chorea. Her experimental animal models also demonstrate that these cross-reactive antibodies can induce changes in behavior further demonstrating that immune responses to CNS components can affect behavior. Dr. David Amaral has very interesting findings using antibodies again CNS components from mothers of individuals with autism spectrum disorders (ASD). Passive transfer of the IgG fraction of antibody from ASD mothers into rhesus monkeys (gestationally treated) resulted in monkeys that were hyperactive and had increased stereotypies. This session should provide a summary and tutorial of the immune system, immune responses and how immune responses to CNS components can affect behavior.

135.00 Immune System, Immune Response and CNS Autoimmune Disease: How They All Come Into Play. R. S. Fujinami*, *University of Utah School of Medicine*

The etiology and pathogenesis of autism is still not known after decades of investigation. Autism is a complex developmental disorder that includes deficits in social interactions and communication as well as restricted and stereotypic behaviors. A potential contributing factor is an immune response to antigens found in the central nervous system (CNS). This immune response could occur

at some point during gestation or early postnatally, and the immune response could be induced either in the mother or in the infant itself. This talk will provide an overview of the immune system and describe autoimmune disease. In addition, how the immune response is generated, what cells participate and how these cells and/or products produced by these cells, such as antibodies, can initiate immunopathology in the CNS will be discussed.

135.01 Maternal Antibodies and Cognitive Dysfunction in the Offspring. B. Diamond[1], J. Y. Lee[2], E. Bertini[1], P. T. Huerta[3], B. T. Volpe*[3] and C. Kowal[1], (1)*The Feinstein Institute for Medical Research*, (2)*Albert Einstein College of Medicine*, (3)*Weill Medical College of Cornell University - Burke Institute*

A subset of anti-DNA antibodies present in the serum of patients with systemic lupus cross-reacts with the NR2A and NR2B subunits of the NMDA receptor (NMDAR). The presence of these antibodies in cerebrospinal fluid of patients correlates with central nervous system manifestations of disease. Furthermore, these antibodies can be eluted from brain tissue of lupus patients.

Studies in cultured cells and in mice show that the antibodies function as receptor co-agonists synergizing with glutamate to activate NMDARs. As co-agonists, they can mediate excitotoxic neuronal death. In vivo models demonstrate that these antibodies can alter either memory function or behavior if they can penetrate the blood-brain barrier and access the hippocampus or amygdala, respectively.

Because it has been reported that the children of mothers with lupus have a 2-5 fold increased incidence of learning disabilities, we asked whether anti-DNA, anti-NMDAR, cross-reactive antibodies might alter fetal brain development when maternal antibodies access fetal brain without the impediment of an intact, mature blood-brain barrier. These antibodies cause discrete impairments in cognitive tasks that require an intact parietal/frontal cortex in mice that were exposed to them in utero. These studies demonstrate that maternal antibodies can alter fetal brain development and cause long lasting impairments in brain function in offspring. The spectrum of antibodies potentially damaging to the developing fetal brain must be determined as well as the conditions that might be explained by this paradigm.

135.02 Molecular Mimicry, Autoimmunity and Infection: Sydenham Chorea and Related Disorders. M. W. Cunningham*[1], C. A. Kirvan[2], L. Brimberg[3], A. Mascaro-Blanco[1], K. Alvarez[1], J. S. Heuser[1], J. F. Leckman[4], S. E. Swedo[5], P. Lombroso[4] and D. Joel[3], (1)*University of Oklahoma Health Sciences Center*, (2)*California State University*, (3)*Tel Aviv University*, (4)*Yale University School of Medicine*, (5)*National Institute of Mental Health, National Institutes of Health*

Sydenham chorea is an autoimmune sequelae which follows group A streptococcal infection and is the major neurologic manifestation of acute rheumatic fever. Neurologic symptoms may result from crossreactive autoimmune responses against brain and group A streptococcal antigens. Human monoclonal antibodies (mAb) derived from Sydenham chorea crossreacted with group A streptococcal antigen and caudate putamen tissue as well as brain antigens lysoganglioside and tubulin. mAb and acute Sydenham chorea sera or CSF targeted human neuronal cells leading to activation of calcium-calmodulin dependent protein (CaM) kinase II and dopamine release. Sera from other streptococcal diseases did not demonstrate such increased antibody reactivity with brain or activation of CaM kinase II. Primary neuronal cells from striatal tissue demonstrated increased CaM kinase II activity when reacted with acute Sydenham chorea sera or CSF. Our recent evidence suggests that dopamine D2 receptors are targeted by the chorea-derived anti-brain mAbs and sera. Serum antibodies from Pediatric Autoimmune Neurologic Disorder Associated with Streptococci (PANDAS) with obsessive compulsive behaviors, vocal tics or tic-like movements demonstrated activation of CaM kinase II at an intermediate level and reactivity with lysoganglioside and dopamine D2 receptor. Comparison of matched acute and convalescent PANDAS sera taken before and during exacerbations demonstrated an elevation in CaM kinase II activity associated with disease. Study of an animal model revealed that immunization with group A streptococcal antigen led to behavioral changes which correlated with antibody deposition in the striatum as well as reactivity of serum IgG with dopamine receptors and the induction of CaM kinase II activity. Our data are consistent with the hypothesis that PANDAS, Sydenham chorea, and some cases of TS may be due to immunologically mediated increases in central dopamine levels and selective activation of central dopamine D2 receptors which combine to produce the neuropsychiatric symptoms seen in these disorders.

135.03 Studies of a Possible Autoimmune Etiology of Autism. D. G. Amaral*[1] and J. Van de Water[2], (1)*University of California, Davis*, (2)*University of California at Davis*

My presentation summarizes the results of collaborative studies between our laboratory and the laboratory of Dr. Judy Van de Water at the M.I.N.D. Institute and Center for Children's Environmental Health at UC Davis. Initial studies by Dr. Van de Water and colleagues were designed to characterize potential immunological dysfunction in children with autism. Among the many abnormalities that have been discovered for at least some children with autism are indications of abnormal autoimmune responses. Van de Water and her students found that approximately 20% of children with autism demonstrate abnormal autoantibodies directed at mature brain tissue. Work carried out by Dr. Sharifia Wills in our laboratory has determined that at least some of these abnormal antibodies identify classes of GABAergic neurons in the cerebellum and other brain regions. I will present evidence indicating the types of staining produced by these antibodies in tissue throughout several brain regions from macaque monkeys. Van de Water and colleagues have also identified autoantibodies in about 12% of women who have had children with autism that are directed at fetal brain tissue. This raised the possibility that at least one cause of autism may be the transplacental transfer of these antibodies to the fetal brain leading to brain damage and the onset of autistic symptoms. Dr. Lorne Martin, a postdoctoral fellow in our laboratory, in collaboration with members of the Van de Water laboratory, conducted a study in which these antibodies were purified and injected into pregnant rhesus monkeys. The behavior of the offspring of these animals was then studied from birth for approximately 1 1/2 years. A striking observation about the animals that received the autism IgG but not IgG from mothers of typically developing children is that they developed profound stereotypies across many behavioral settings and evaluations. I will discuss these studies related to a maternal autoimmune etiology of autism and their implications for the detection of one class of risk factors and briefly describe our ongoing replication studies.

Oral Presentations Program
136 Neuroimaging - Connectivity

136.00 Abnormal Functional Connectivity during Emotional Face Processing Is Associated with Neural Abnormalities in the Amygdala in Autism Spectrum Disorders. N. M. Kleinhans*[1], C. Johnson[1], T. L. Richards[1], J. Greenson[1], E. H. Aylward[1] and G. Dawson[2], (1)*University of Washington*, (2)*Autism Speaks, UNC Chapel Hill*

Background:

Difficulty evaluating and interpreting facial expressions has been reported in autism spectrum disorders (ASD) and is thought to be associated with amygdalar abnormalities. Despite numerous brain imaging studies of amygdala response to emotional faces in ASD, the relationship between the integrity of the neural tissue and neural functioning of the amydgala has not been previously assessed.

Objectives:

Functional magnetic resonance imaging (fMRI) and proton magnetic resonance spectroscopy (MRS) were used to explore the neural basis of abnormal emotional face processing in ASD.

Methods:

MRS and fMRI data were collected within the same scanning session. During fMRI scanning, 29 individuals with ASD and 25 normal controls viewed Ekman faces depicting fear or anger. Subjects were instructed to select which of two faces at the bottom of the screen portrayed the same emotion as the face at the top of the screen. The control condition consisted of a simple shape-matching task. The left amygdala was used as the seed region for the functional connectivity analyses. A physiological interaction approach was utilized to identify regions that showed stronger connectivity during the emotional face processing task compared to the shape matching task. MRS was used to measure n-acetyl aspartate (NAA), creatine/phosphocreatine (Cre), and choline/choline containing compounds (Cho) in the left amygdala. Automated tissue segmentation on the MRS voxel yielded percent white matter, gray matter, and CSF. Metabolite levels were normalized to 100% brain tissue by controlling for percentage of CSF within the voxel.

Results:

For the comparison of emotional faces vs. shapes, controls evidenced significantly stronger connectivity between the amygdala and right fusiform gyrus and the amygdala and left prefrontal cortex. The ASD group showed

significantly increased connectivity between the amygdala and the occipital lobe (BAs 17, 18, and 19). Functional connectivity analyses were also conducted with the metabolite concentrations entered as independent variables. Percentage of gray matter within the MRS voxel was entered as a covariate in the analyses. For the ASD group, greater functional connectivity from the amygdala to the right fusifrom gyrus and right prefrontal cortex was associated with higher concentrations of Cre. Increased functional connectivity from the amygdala to the right fusiform, left hippocampus, left prefrontal cortex, and bilateral occipital cortex was associated with higher concentrations of NAA. No significant correlations between functional connectivity and Cho concentrations were observed.

Conclusions:

Overall, these findings indicate that individuals with ASD exhibit reduced connectivity to prefrontal regions and the fusiform face area and increased connectivity to primary and secondary visual cortices during socioemotional processing. The correlation between metabolite levels (NAA and Cre) and functional connectivity between the amygdala and cortical regions suggests that abnormal connectivity in ASD may be associated with neuronal impairments related to the integrity and energetic status of the cells. Other possible underlying neuronal abnormalities such as gliosis or chronic inflammation are less likely to contribute to abnormal connectivity given the current findings.

136.01 A MEG Study of Functional Connectivity during Preparation for Saccades in ASD. T. Kenet*[1], E. V. Orekhova[2], N. Shetty[1], A. K. Lee[3], M. Vangel[1], M. Elam[2], M. Herbert[1], M. S. Hämäläinen[1] and D. S. Manoach[4], (1)*Massachusetts General Hospital*, (2)*Sahlgrenska University Hospital*, (3)*Massachusetts General Hospital-Harvard Medical School*, (4)*Harvard Medical School*

Background: A significant body of evidence has accumulated in support of the cortical hypo-connectivity hypothesis of autism; the hypothesis states that individuals with autism spectrum disorders (ASD) have weaker than normal long-range cortical functional connectivity that may contribute to their cognitive abnormalities. Our own studies show that individuals with ASD (1) make more errors than controls on an antisaccade task, and (2) when preparing for a saccade, show widespread reduced connectivity in the alpha band relative to controls.

Objectives: To investigate whether the reduced functional connectivity in ASD that we observed in the alpha band is task and region specific. In particular, given the higher error rate in the ASD group for antisaccades, we investigated whether group differences in coherence were more pronounced during preparation for a more cognitively demanding task (an antisaccade) than for a simple task (fixation or a prepotent prosaccade), and if so, which cortical regions were most affected.

Methods: We studied 10 high functioning adults with ASD and 10 age and gender matched healthy controls using whole head Magnetoencephalography (MEG). We looked at three conditions – 1) fixation with no immediate associated task ('fixation'), and fixation in preparation for 2) a saccade towards a suddenly appearing visual stimulus ('prosaccade') or 3) a saccade away from the stimulus ('antisaccade'). For each subject and condition, we analyzed the MEG amplitude and coherence in source space (i.e., cortical space), in the peak alpha frequency, during the preparatory interval in between the instructional cue and stimulus appearance. We focused on coherence between ocular motor regions that have been found to show preparatory activity for saccades: the inferior and superior portions of the frontal eye field (FEF), the supplementary eye field (SEF), and intraparietal sulcus (IPS).

Results: Multiple regions showed evidence of task-dependent group differences in functional connectivity in the alpha frequency band: (1) It has been shown that top-down connections suppress activity in visual cortex in preparation for an antisaccade relative to prosaccades. We observed significantly greater suppression in the control group. (2) Relative to fixation, task-related increases in coherence were observed in the control group between the FEF and the SEF and a parietal region overlapping with the IPS, areas critically involved in saccades. No reliable task-related increases in coherence were observed in the ASD subjects. Finally, (3) in the control group, there was a trend for slightly increased coherence between the right and left FEFs during preparation for antisaccades relative to prosaccades, but no such trend was observed in the ASD group.

Conclusions: Our data indicates that when preparing for a saccade, participants in the control group modulate (both increase and suppress) alpha activity and coherence across the saccadic network according to task difficulty. There appears to be no or little such modulation in the ASD group, potentially due to reduced functional connectivity. Such lack of modulation of the coherence may reduce top-down control over volitional saccades and could contribute to the observed increased antisaccade errors and faster correct responses (i.e., a disruption of the speed-accuracy trade-off).

136.02 Alterations in Frontal Lobe Tracts and Corpus Callosum in Young Children with Autism Spectrum Disorder. A. Kumar, S. K. Sundaram, L. Sivaswamy, M. E. Behen*, M. I. Makki, J. Ager, H. T. Chugani and D. C. Chugani, *School of Medicine, Wayne State University*

Background:

It has been suggested that autism spectrum disorder (ASD) may be a disorder of brain networks, rather than associated with dysfunction in discrete brain regions and a number of studies have found abnormalities in the brain white matter, particularly in frontal lobe and corpus callosum.

Objectives:

In the present study, we used magnetic resonance diffusion tensor imaging (DTI) to investigate the major association tracts of the frontal lobe and the corpus callosum in young children with ASD.

Methods:

Thirty-five children with ASD (mean age: 5.1 years; range: 2.3-8.8 years, 30 males and 5 females) and 16 typically developing children (mean age: 5.5 years; range: 2.5-8.6 months, 12 males and 4 females), underwent neuropsychological evaluation and DTI. The uncinate fasciculus (UF), inferior fronto-occipital fasciculus (IFO), arcuate fasciculus (AF), cingulum (Cg), and corpus callosum (CC) were isolated using DTI tractography and fractional anisotropy (FA), apparent diffusion coefficient (ADC), mean fiber length, mean fiber volume and mean fiber density were calculated for each fiber tract. In order to independently confirm the results (FA, ADC) obtained by tractography, we also performed tract based spatial statistics (TBSS), an automated, operator-independent voxel-wise analysis, of brain white matter.

Results:

Right UF (p=0.02), bilateral IFO (p=0.04 for both left and right), left AF (p=0.01), right Cg (p=0.04) and CC (p=0.03) had significantly decreased FA in ASD group compared to controls. Right AF was found to have significantly increased diffusivity (ADC) in ASD group compared to controls (p=0.04). TBSS analysis also revealed that the voxels in the regions of bilateral UF, IFO, AF, right Cg and CC had significantly different FA between the two groups (reduced FA in ASD group). Left UF showed shorter fiber length (p=0.008), while right UF had significantly longer fiber length (p=0.04), increased fiber volume (p=0.01) and higher fiber density (p=0.006) in ASD group compared to controls. There was also a reversed pattern of asymmetry in average fiber length (p=0.001) and fiber density (p=0.006) of the UF in the ASD group compared to controls: average fiber length and fiber density of the right UF was higher than those of the left UF in the ASD group, whereas this pattern was opposite in controls. CC, in ASD group, had significantly longer fiber length (p=0.008) with higher fiber density (p=0.009). Left Cg was also found to have significantly higher fiber density in the ASD group (p=0.02). There was also difference in the fiber length distribution of right UF and right AF between the two groups. Whereas, both right UF and right AF had bi-modal distribution of fiber length in controls, the right UF had a significantly larger second peak (fiber distribution skewed to the right; p=0.009) and the right AF was uni-modal and sharper (right skewed; p=0.03) in the ASD group, indicating more longer fibers in these tracts.

Conclusions:

We found qualitative and quantitative abnormalities in frontal lobe white matter tracts and corpus callosum in young children with ASD, which may indicate developmental dysregulation of neuronal connectivity.

136.03 The Limbic System in the Asperger Syndrome: a Preliminary Diffusion Tensor Tractography Study. L. Pugliese*[1], M. Catani[1], M. Thiebaut de Schotten[1], C. Murphy[1], E. Daly[2], D. Murphy[1] and .. MRC UK AIMS Network[1], (1)*King's College*

London, Institute of Psychiatry, (2)*Institute of Psychiatry, King's College London*

Background: It has been suggested that people with Autistic Spectrum Disorder (ASD) have altered development (and connectivity) of limbic circuits[1,2]. However, direct evidence of anatomical differences specific to white matter pathways underlying social behavior and emotions in ASD, is lacking.

Objectives: We used Diffusion Tensor Imaging (DTI) tractography to compare, in vivo, tract-specific measurements along the principal limbic pathways between people with Asperger syndrome and healthy controls.

Methods: We recruited 66 people: twenty-four males with Asperger Syndrome (mean age 23±12 years, age range: 9-54 years) and 42 age-matched male controls (mean age 25±10 years, age range: 9-54 years). DTI were acquired on a 1.5 T GE Signa NV/i LX (General Electric, Milwaukee, WI) and processed as described by Jones at al[3]. We quantified tract-specific diffusivity measurements as indirect indexes of tract volume (e.g. number of streamlines) and micro-structural organization and integrity (e.g. mean diffusivity, MD; and fractional anisotropy, FA) of the main limbic tracts. These include the inferior longitudinal fasciculus (ILF), inferior frontal occipital fasciculus (IFOF), uncinate, cingulum and fornix.

Results: ***DTI measurements***. *Streamlines*: People with Asperger syndrome had a significantly higher number of streamlines in the right (p=0.003) and left (p=0.03) cingulum and in the right (p=0.03) and left (p=0.04) inferior longitudinal fasciculus. In contrast people with Asperger syndrome had a significantly lower number of streamlines in the right uncinate (p=0.02). The number of streamlines for the right (but not for the left) cingulum survived Bonferroni correction. *Mean Diffusivity:* The Asperger group showed significantly increase in the ILF bilaterally, and in the right cingulum and in the right IFOF. *Fractional anisotropy:* individuals with Asperger syndrome had a significant decrease in FA within the IFOF bilaterally, and in the right uncinate fasciculus. ***Age-related differences.*** *Streamlines:* There were no significant age-related differences between groups. *Mean diffusivity:* There was statistically significant age-related difference in mean diffusivity of the left uncinate fasciculus (Zobs=2.05) (p=0.02). *Fractional Anisotropy:* There were no age-related between-group differences.

Conclusions: People with Asperger syndrome have significant differences in micro-structural integrity (and maturation) of some, but not all, limbic pathways. This may mostly affect (respectively) the cingulum and uncinate fasciculus. Our findings support previous reports of anatomical, metabolic and functional differences in the limbic regions of people with Asperger and may explain some of the social and emotional[4,5] anomalies typically found in the disorder. Further studies linking the involvement of these pathways are required.

References: ***1)*** Courchesne E,et al. Curr. Opin. in Neurobiology. 2005;15(2):225-230. ***2)*** Jones D. Hum.Brain Mapp. 2002;15(4):216-30 ***3)*** Wickelgren I. Science. 2005;308(5730):1856-8. ***4)*** Damasio AR. Arch Neurol. 1978;35(12):777-86. ***5)*** Mundy P. J Child Psychol Psych. 2003;44(6):793-809.

136.04 Probabilistic DTI Tractography Shows Compromised Connectivity Between Regions of Atypically Increased Activity in Children with Autism Spectrum Disorder. D. K. Shukla*[1], B. Keehn[2], A. J. Lincoln[3] and R. A. Müller[1], (1)*San Diego State University*, (2)*San Diego State University / University of California, San Diego*, (3)*Alliant International University*

Background:

Previous studies have shown white matter compromise in children and adults with autism spectrum disorder (ASD), which may relate to reduced connectivity and impaired function in distributed networks. However, tract-specific evidence remains limited in ASD.

Objectives:

To examine connectivity between regions with atypically increased activity during visual search in children with ASD, using probabilistic white matter fiber tracking.

Methods:

Diffusion tensor imaging (DTI) data of 17 children with ASD and 13 typically developing (TD) children were acquired from a 3T MRI scanner, using single-shot diffusion-weighted EPI pulse sequence with two degrees of diffusion weighting

(b=0 and 2000 s/mm^2, 15 non-linear directions, four repetitions). Geometric distortions due to local magnetic field inhomogeneities were corrected using field maps.

Diffusion tensor tractography was performed using a probabilistic tracking approach from two regions of interest (ROIs) identified from a corresponding fMRI study, which showed atypically increased activation in ASD group in an fMRI study of visual search. Tracts were determined for pairs between a seed ROI in occipital white matter and four secondary ROIs in parietal and frontal lobes. Bayesian estimation of diffusion parameters using Markov Chain Monte Carlo sampling techniques and trilinear interpolation of the probability density functions were employed to determine the streamline between given ROIs. Volume and integrity of identified tracts were determined.

Results:

Significant group differences were detected for tract volume, fractional anisotropy (FA), mean diffusivity (MD), and radial diffusion. In the ASD group, FA was significantly lower (0.18+/-0.007 for ASD vs. 0.23+/-0.01 for TD, p=0.003); mean diffusivity was significantly higher (0.8+/-0.001 vs. 0.7+/-0.001 *10^{-3} mm^2/s, p=0.002), as was radial diffusion (0.7+/-0.001 vs. 0.6+/-0.001 *10^{-3} mm^2/s, p=0.008). Significantly decreased tract volume in ASD was also found (33078+/-16691 vs. 159237+/-36837 mm^3, p=0.002).

Conclusions:

These results suggest that increased task-related regional activation may be accompanied by impaired network connectivity in children with ASD. Activation in atypical sites, as reported in previous fMRI studies of ASD, may therefore reflect isolated or 'disconnected' activity. Significantly higher radial diffusion in our ASD group may specifically suggest disruption of myelin sheaths responsible for maintaining axonal integrity.

136.05 Relationships Between Diffusion Tensor Imaging and the Social Responsiveness Scale. A. L. Alexander*[1], J. E. Lee[1], M. K. Chung[1], M. DuBray[2], P. T. Fletcher[2], A. Froehlich[2], E. Bigler[3], J. E. Lainhart[2] and N. Lange[4], (1)*University of Wisconsin*, (2)*University of Utah*, (3)*Brigham Young University*, (4)*Harvard University*

Background: The social responsiveness scale (SRS) is a quantitative summary measure of key autism trait features with an emphasis on social impairments. Recent neuroimaging studies using diffusion tensor imaging (DTI) have found microstructural differences between autistic and typically developing children and young adults.
Objectives: The main objectives were to investigate whether there were relationships between the SRS score and DTI measures and to determine the brain locations that appear to be related to the SRS.
Methods: High resolution DTI data were collected using at 3T scanner in 37 high functioning individuals with autism and 27 control subjects. The groups were matched for age (range: 7-33 years), handedness, total IQ, and head circumference. SRS values were obtained for all subjects. For most subjects, the SRS was obtained using a parental report, although in seven of the control adult subjects, the SRS was derived using a self-report. Maps of DTI measures were computed including the fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD). State-of-the-art voxel-based analysis was performed to assess the relationships between the DTI measures and the SRS scale across all subjects. Nonlinear warping was used for between-subject image registration to achieve optimal spatial correspondence. A general linear model with both age and SRS as independent variables was used for statistical testing. A corrected $p < 0.05$ threshold was used to report regions of significant relationships.
Results: Significant relationships were observed between the SRS and the FA, MD and RD diffusion measures. FA appeared to negatively correlated to SRS in the genu and body of the corpus callosum, left superior temporal gyrus, bilateral superior longitudinal fasciculus, posterior cingulum bundles, and right prefrontal white matter. Both MD and RD appeared to be positively correlated to SRS in similar regions plus bilateral thalamus and temporal stem regions. The RD measure showed the most significant correlations.
Conclusions: This study suggests a relationship between a quantitative measure of autism traits (the SRS) and tissue microstructure as assessed with DTI. These effects were observed in diffuse white matter regions, suggesting that there may be a relationship between white matter abnormalities and autism traits. The specific mechanisms of the DTI changes in white matter

associated with autism remain unclear.
Sponsors: The project described was supported by Grant RO1s MH080826 and MH62015 from the National Institute Of Mental Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute Of Mental Health or the National Institutes of Health. Past data collection was supported in part by NICHD/NIDCD U19 HD035476, part of The Collaborative Program of Excellence in Autism.

Oral Presentations Program
137 Diagnosis/Behavior

137.00 The Toddler Version of the Autism Diagnostic Interview-Revised (Toddler ADI-R): New Algorithms. S. H. Kim* and C. Lord, *University of Michigan*

Background: The ADI-R is a standardized, semistructured, investigator-based interview for caregivers of autistic individuals, which provides diagnostic algorithms for the ICD-10 definition of autism (World Health Organization [WHO], 1992) and DSM-IV (American Psychiatric Association [APA], 1993). The interview focuses on the three domains of functioning – language/communication; reciprocal social interactions; and restricted, repetitive, and stereotyped behaviors and interests. The Toddler-ADI-R exists in a research version, which includes additional questions about early development and symptom onset with total 132 questions. The algorithms for the ADI-R have been used for children administered Toddler-ADI-R since the Toddler-ADI-R does not provide its own algorithms.

Objectives: In an effort to develop the Toddler-ADI-R algorithms appropriate for younger children, the sensitivity and specificity of individual items have been explored in differentiating children with ASD clinical diagnoses from children with other nonspectrum disorders and children with typical development. Exploratory and confirmatory factor analyses, building on recent work on the ADI-R, will be described as well.

Methods: Analyses were conducted using a dataset of ADI and psychometric scores for 624 cases children aged 10 to 63 months (mean age=31.87). 259 cases were derived from children with autism; 156 from children with PDD-NOS; 127 from children with various non-ASD developmental delays (DD); 82 from children with typical development (TD). ADI item distributions were compared by diagnosis, and items with high sensitivity and specificity were identified. These items will be included in exploratory and confirmatory factor analyses for the development of the Toddler-ADI-R algorithms.

Results: We identified 37 items that showed high specificity and sensitivity. There were12 items on which fewer than 20 % of children with autism scored 0 and not more than 20 % of children with DD and TD scored 2 or 3. 25 additional items were identified with more lenient criteria. 29 of these 37 items are included in the standard ADI-R algorithm (though as "ever" or most abnormal 4 - 5 codes). Several items not included in the original ADI-R algorithms showed high specificity and sensitivity for the children in the present study: *sharing others' pleasure and excitement, non-speech vocalization, elicited vocal imitation, greeting, social crying, affection, initiation of appropriate activities.*

Conclusions: The items identified here will be included in the analyses for the development of the new Toddler-ADI-R algorithms to improve the diagnostic validity of the instrument.

137.01 Comparison of Diagnostic Classification Between the WPS and Revised ADOS Modules. A. P. Thompson*[1], P. Szatmari[1], S. E. Bryson[2], E. Fombonne[3], P. Mirenda[4], W. Roberts[5], I. M. Smith[2], T. Vaillancourt[6], J. Volden[7], C. Waddell[8], L. Zwaigenbaum[7], S. Georgiades[9], .. Pathways in ASD Study Team[9] and E. Duku[1], (1)*Offord Centre for Child Studies, McMaster University*, (2)*Dalhousie University/IWK Health Centre*, (3)*McGill University*, (4)*University of British Columbia*, (5)*University of Toronto*, (6)*University of Ottawa*, (7)*University of Alberta*, (8)*Simon Fraser University*, (9)*Offord Centre for Child Studies & McMaster University*

Background: The Autism Diagnostic Observation Schedule (ADOS; Lord et al. 2000) assesses communication, social and play skills, and restrictive/repetitive behaviours in the diagnosis of ASD. Recently, Gotham et al. (2007, 2008) revised the algorithms for Modules 1, 2 and 3 to improve diagnostic validity and to allow for increased comparability across modules. Two algorithms were derived for Module 1 ("no words," "some words"), two for Module 2 ("younger than age 5," "age 5 years and older"), and one for Module 3 as dividing this sample by age or language level did not result in more homogeneous groups.

Objectives: To assess agreement on ASD sub-types (autism/ASD) based on the WPS-published algorithms relative to the revised algorithms in a sample of preschool children with ASD participating in a Canadian longitudinal study.
Methods: ADOSs were administered on enrolment (Time 1 n=329; 262 Module 1, 63 Module 2, 4 Module 3) and again one year later (Time 2 n=171; 84 Module 1, 69 Module 2, 18 Module 3). Classification as autism, non-autism ASD (hereafter ASD) and non-ASD was determined with the WPS and revised algorithms at both time points. Crude agreement and kappa values (that take chance into account) were calculated.
Results: At T1, the frequency of autism and ASD was 82% and 18% using the WPS algorithms and 91% and 9% using the revised algorithms. A few children (n=10) shifted from autism to ASD or from ASD to non-ASD when the revised Module 1 "no words" algorithm was applied. However, for all other algorithms, if a child changed diagnostic categories when the revised versus WPS algorithm was used, the shift was toward a more severe diagnosis (ASD to autism, non-ASD to ASD/autism) both at T1 and T2. Kappa (agreement between algorithms) at T1 was .40. At T2, the frequency of autism diagnoses decreased for both algorithms relative to T1. However, it was still higher for the revised (85%) algorithms compared to the WPS (71%) algorithms. Kappa at T2 was .52. ADOSs were administered at T1 and T2 for 169 children, allowing examination of change in diagnostic categories. In this sub-sample, probability of a diagnosis of autism was higher at T1 and remained high at T2 for the revised algorithms relative to the WPS algorithms. Agreement in an autism classification between T1 and T2 was 87% for the WPS algorithms and 90% for the revised algorithms. Given the high rate of autism, weighted kappas were computed.
Conclusions: The revised algorithms were intended to provide a more accurate differentiation of autism/ASD from non-ASD children by being less sensitive to variability in age and language ability. This change is accompanied by a shift in diagnostic classification when the revised versus the WPS algorithms were applied, from a less (ASD) to more severe (autism) diagnostic category. This has implications for researchers who may wish to assess phenotypic heterogeneity within the ASD continuum or to measure change over time in diagnostic status. The revised algorithms may be less sensitive to heterogeneity and change over time in ASD behaviours.

137.02 Diagnosis of Autism Spectrum Disorder: a Study of Community Practice. N. Akshoomoff*[1], C. Corsello[1] and A. Stahmer[2], (1)*University of California, San Diego*, (2)*Rady Children's Hospital*

Background: Longitudinal research studies have demonstrated experienced clinicians using standardized assessment measures can make a reliable diagnosis of ASD in children under age 3. Limited data are available regarding the sensitivity and specificity of these measures in community settings.

Objectives: To characterize the practices of a group of community clinicians who evaluate young children for developmental disorders and investigate the agreement between clinical judgment and results from standardized diagnostic measures in a community sample.

Methods: Clinical records for 145 children seen for possible ASD or social/language concerns were examined. The children (125 males and 20 females) were between 24 and 36 months of age (M = 30.2 months, S.D. = 3.2). An IQ estimate was available for 91% of the children (overall mean IQ= 71.64, S.D.=16). Classification results obtained from standardized diagnostic measures were compared with clinical final diagnosis. A standard method of record review based on the MADDSP protocol was also used to examine the diagnostic descriptions and the specific behaviors/symptoms that clinicians included in the reports. Reviewers using this method were blind to classification results from the diagnostic measures and clinical diagnosis.

Results: During the 23-month period that was examined, the Autism Diagnostic Observation Schedule (ADOS) was used with 123 (85%) children and the Social Communication Questionnaire (SCQ) was adopted at a later time and used with 61 children (42%). Across the three diagnostic categories (autistic disorder, PDD-NOS, or nonspectrum), the ADOS had good sensitivity (.95) and specificity (.88). The SCQ had weak sensitivity (.64) but moderate specificity (.82). The Modified Checklist for Autism (M-CHAT) was used with only 27% of the children but had good sensitivity (.88) and weak specificity (.67). For children with a clinical diagnosis of autistic disorder, there was 80% agreement between the ADOS and SCQ or M-CHAT but only 55% for

children with PDD-NOS had agreement between these measures. In 70% of cases without an ASD diagnosis, scores below the cutoff on both types of measures were obtained. There was agreement between clinician diagnosis, record review classification, and reviewer diagnosis across the majority of cases. The majority of discrepancies (70%) were between a clinical diagnosis of PDD-NOS and a record review classification of autistic disorder. Child factors, such as strengths and level of functioning, appeared to account for most of these discrepancies.

Conclusions: These results demonstrate that following best practice guidelines, standardized measures such as the ADOS and SCQ, can be successfully incorporated into clinical practice, have relatively good sensitivity and specificity, and worked well with a referred sample of two-year-olds. The standard record review approach allows for an examination of child characteristics that may influence diagnostic decisions.

137.03 A Multi-Dimensional Model for the Phenotypic Structure of Behaviours, Functional Level and Symptoms in Young Children with Autism. P. Szatmari*[1], S. Georgiades[1], S. E. Bryson[2], E. Duku[1], W. Roberts[3], E. Fombonne[4], P. Mirenda[5], I. M. Smith[2], T. Vaillancourt[6], J. Volden[7], C. Waddell[8], L. Zwaigenbaum[7], A. P. Thompson[1], N. Garon[9] and .. Pathways in ASD Study Team[10], (1)*Offord Centre for Child Studies, McMaster University*, (2)*Dalhousie University/IWK Health Centre*, (3)*University of Toronto*, (4)*McGill University*, (5)*University of British Columbia*, (6)*University of Ottawa*, (7)*University of Alberta*, (8)*Simon Fraser University*, (9)*IWK Health Centre*, (10)*McMaster University*

Background: Autism is neurodevelopmental disorder characterized by symptoms of social and communication impairment and by the presence of repetitive, restricted, stereotyped behaviours. The fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM IV) organizes these symptoms in three distinct, mutually exclusive categories and criteria in each must be met to qualify for a diagnosis of autism. This conceptualization, which is based primarily on clinical judgment, has failed to capture the variability and complexity of the clinical presentation of autism. Recent factor analytic studies support the idea of using a dimensional as well as a categorical approach to conceptualizing autism. However, these studies have focused on a single symptom-based instrument (the Autism Diagnostic Interview Revised; ADI-R) and a single informant.

Objectives: The main objective of this study is to examine the structure of an expanded autism phenotype that, in addition to symptoms, includes information derived from other sources and methods.

Methods: The sample consisted of 255 preschool children with a clinical diagnosis of autism participating in a Canadian longitudinal study (Pathways in ASD). Scores from multiple parent-report and direct observational sources, including diagnostic (ADI-R), language (Preschool Language Scale Fourth Edition; PLS-4), adaptive functioning (Vineland Adaptive Behavior Scales Second Edition; VABS-II), and behavioural (Child Behavior Checklist; CBCL 1.5/5 & Repetitive Behavior Scale Revised; RBS-R) measures were used in exploratory factor analysis.

Results: A three-factor solution explaining 63.70% of the variance was selected based on the scree plot criterion and conceptual interpretability. The three factors were labeled maladaptive behaviours (MB), containing repetitive behaviours and internalizing and externalizing behaviours, general level of functioning (GLF), reflecting adaptive behaviours from the VABS-II and language scores from the PLS-4, and social-communication symptoms (SCS), representing those domains from the ADI-R.

Conclusions: Based on these findings, we propose a new multidimensional model for the phenotypic structure of behaviours, functional level and symptoms in young children with autism. The use of quantitative severity indices on the three latent dimensions (MB, GLF, & SCS) appears to capture the phenotypic diversity of autism in a parsimonious yet comprehensive way.

137.04 Relationships Between Restricted and Repetitive Behaviours and Adaptive Skill Development Over 4-5 Years in Children with ASD. K. Bopp*, P. Mirenda, S. Jull and R. Stock, *University of British Columbia*

Background: A diagnosis of autism spectrum disorder (ASD) requires the presence of restricted and repetitive behaviors (RRBs); however, relatively few studies to date have examined the relationship between this broad category of behaviors and changes in other developmental variables over time. Examination of such relationships may aid in our understanding of the impact of ASD symptomatology on skill acquisition.

Objectives: To examine the relationship between early RRBs and the development of adaptive behavior skills in a cohort of young children with autism who were followed over 4-5 years.

Methods: Longitudinal data were collected for 69 children with ASD (84% males, mean CA=50 months) prior to intervention (T1) and 6 (T2), 12 (T3), 24, 32, and 53 months later, using subscales from the Vineland Adaptive Behavior Scales (VABS). The RRB variable used at T1, T2, and T3 was constructed using cross-test items endorsed by an expert jury. The coefficient alpha for the RRB variable was 0.77, indicating that it was internally consistent with little measurement error. After controlling for chronological age, nonverbal IQ, and autism severity, T1 to T3 RRBs and changes in RRBs over the first 6 and 12 months of intervention were examined as predictors of the developmental trajectories of VABS communication, social, and daily living skills using SAS Proc Mixed analyses.

Results: Children's RRB scores at both T2 (β = -0.033, $t(69) = -2.75$, $p = 0.006$) and T3 (β = -0.026, $t(69) = -2.42$, $p = 0.016$) predicted the development of VABS daily living skills over 4-5 years. In addition, changes in children's RRB scores over the first 6 months of intervention (T2 – T1) predicted the slope of daily living skills over 4-5 years ($\beta = -0.029$, $t(69) = -2.02$, $p = 0.044$). RRBs did not predict the development of either adaptive communication or social skills over time. Overall, children who had higher RRB scores at T2 or T3 had less of an increase in the slope of daily living skills over 4-5 years. In addition, children whose RRBs improved over the first 6 months of intervention had more of an increase in the slope of daily living skills over time.

Conclusions: Past research has found some evidence for a general relationship between RRBs and other variables (e.g., Gabriels, Cuccaro, Hill, Ivers, & Goldson, 2005; Honey, McConachie, Randle, Shearer, and LeCouteur, 2008). This is the first study to find a predictive relationship between early RRBs and the development of daily living skills over a long time period (i.e., 4-5 years). In this study, RRBs included both repetitive stereotypic gross and fine motor behaviors such as hand flapping, rocking, and humming; and insistence on sameness behaviors such as lining up objects and demanding that routines always occur in the same way. It appears that high levels of RRBs negatively affect the acquisition of daily living skills, perhaps because, like RRBs, they involve both gross and fine motor skills and usually occur in a predictable sequence (e.g., hand washing, dressing).

137.05 Facilitating Behavioral Change: a Parent Based Program. M. McCreadie and A. McGauley*, *National Autistic Society*

Background: Families of children with Autism Spectrum Disorders (ASD's) face unique stressors (Gray and Holden 1992). Studies show that the greatest predictors of parental stress are variables associated with the behaviour, age and size of their child (Rousey *et al*. 1990; Bromley & Blacher 1991; Kobe *et al*. 1991; Blacher *et al*. 1992).
Given the benefits evidenced in literature of parent programmes (Tonge et al 2006), there is surprisingly little written about the variables which both facilitate and obstruct the implementation of such programmes, (Johnsone & Hastings 2001). While many home-based psycho-educational interventions focus on teaching parents' skills for managing their child's behaviour they take little account of coping styles used by parents in challenging, low-control situations (Mc Eachin et al, 1993).

Objectives: The current study is collaboration between the National Autistic Society and the Scottish Government evaluating the impact of a parent based psycho-educational programme. It hypothesises that by taking account of the dynamic relationship between stress and coping (Folkman and Lazarus, 1984) parents are more likely to establish behavioural change in their child while moderating their own stress.
The study consisted of 2 workshops delivered 6 months apart covering; understanding autism, appraising behaviour, behaviour management, sensory issues, fear stress and anger, and obsessive and ritualistic behaviour. Following each workshop, participants were issued a manual providing a more in depth discussion of the points covered as well as practical techniques to apply with their child. The manual also utilised aspects of cognitive reframing techniques to assist parents in appraising their child's behaviour and associated stressful encounters.

Methods: Using measures of stress (Parental Stress Index; Abidin,1995) and coping (Ways of Coping revised; Lazarus and Folkman, 1985), the study examined the impact of 2 the workshops

and their associated manuals on > 90 families over 12 months sampled from 3 local government areas across Scotland. In addition 20 families were selected from each local authority cohort and given 21 hours of contact with facilitators trained in Motivational Interviewing Techniques (Miller & Rollnick, 1991). Local government area Cohorts were identified to control for distribution across a number of demographics. Participants were parents of school aged children, with families being selected for facilitator involvement based on stress scores in the child domain of the Parenting Stress Index. The Study used an A-B design format, taking measures of stress and coping across the timescale of the intervention, with other qualitative measures used to assess the impact of the workshops alone.
Results:

Narratives were recorded from parents, and preliminary findings using statistical analysis suggest changes in appraisal of stressful encounters. Furthermore, an earlier study by one of the authors which evaluated the workshop and manual alone suggests a statistically significant result for individuals adapting their coping style relative to the appraised controllability of the situation.
Conclusions: The study suggests that a goodness-of-fit approach (Terry & Hynes 1998) to stress appraisal and coping within this population of parents is likely to have more favourable outcomes when implementing any psycho-educational programme.